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IN THE COURT OF ARBITRATION FOR SPORT

IN THE MATTER OF FLOYD LANDIS,

CAS 2007/A/1394

FLOYD LANDIS V. UNITED STATES ANTI-DOPING AGENCY

DECLARATION OF KEITH GOODMAN

I, Keith Goodman, declare and state as follows:

1. I am over the age of 18 and have personal knowledge of the following facts and, if called as a witness, could and would competently testify to them.

2. I have a Ph.D. in nutritional biochemistry with a minor in analytical chemistry with specific expertise in isotope ratio mass spectrometry. I manage the day-to-day operations of a pharmaceutical research laboratory. The details of my professional career are further described in my CV, which is attached to this declaration as Exhibit 1. However, by way of summary, my experience in the field of analytical chemistry, and specifically, isotope ratio mass spectrometry is as follows:

a. I am currently a Senior Director of Analytical Chemistry at Xanthus Pharmaceuticals in Cambridge, MA and manage a state-of-the-art pharmaceutical research laboratory. In this capacity, I have (1) designed and executed *in vitro* (with purified cell fractions) and *in vivo* (animal) metabolism experiments to evaluate pharmacokinetics (metabolism and exposure) of drugs and (2) developed assays using high performance liquid chromatography (HPLC) and liquid chromatography tandem mass spectrometry (LC MS/MS) to analyze samples from *in vivo* and *in vitro* experiments.

b. I have previously managed a stable isotope laboratory for Boyce Thompson Institute for Plant Research, in Ithaca, NY.

c. I am familiar with and have used several different types of isotope ratio instruments and other analytical instruments, including the API 4000 tandem mass spectrometer coupled to an Agilent HPLC system used for structural confirmation and quantitative analysis, a Waters HPLC system, an Agilent MSD GC MS for structural

confirmation and quantitative analysis, a Finnigan MAT 252 with GC combustion interface for isotope ratio analysis of mixtures of volatile organic molecules, a Finnigan Delta S with a Gilson autosampler for gas and headspace gas analysis and a tube cracker interface for isotope analysis of samples prepared offline, a VG Optima with GC Isochrom II interface (for online combustion of volatile organics), a Carlo Erba elemental analyser for bulk analysis of solids and liquids, a Finnigan MAT Delta Plus with a Conflo II interfaced to a Carlo Erba NC2500 elemental analyzer, the Europa Geo 20-20 dual-inlet gas isotope ratio mass spectrometer with an ANCA-SL elemental analyzer and an ANCA-TG for trace gas measurements, and a Finnigan BreathMAT IRMS for isotopic analysis of breath CO_2.

d. I have served as an expert witness/consultant to the US Track and Field Association in 1999 following an alleged testosterone doping violation. The T/E ratio was borderline elevated at T/E 7.4 (the threshold was 7 at the time) so the IRMS test was used as final confirmation. The subsequent IRMS data was interpreted as positive. I then audited the preparation and CIR re-analysis of the athlete's "B" sample at Dr. Schantzer's laboratory in Cologne. Over the following few weeks, I worked with the lawyers to assemble the findings for the International Association of Athletics Federations (IAAF) arbitration in Monaco.

e. I have years of hands on experience with the gas chromatography combustion isotope ratio mass spectrometry (GC-C-IRMS) and have authored several papers that deal with the analytical performance and limitations of these systems. These include issues of peak overlap and resolution, which are critical in obtaining reliable isotope ratio measurements.

f. I am very familiar with the analytical parameters known as retention time and relative retention time from my work in managing and operating analytical and stable isotope laboratories and because they are crucial to accurate results in chromatography and specifically, isotope ratio calculation.

g. I am very familiar with issues involving the quality of chromatograms and matrix interference, including co-eluting contaminant peaks, inadequate peak detection and integration algorithms. I am very familiar with the impact these issues may have in the case of biologically derived samples (i.e. urine, plasma, or tissues).

3. The use of Gas Chromatography Combustion Carbon Isotope Ratio Mass Spectrometry is a well-established method for determining the isotopic value of target substances. In order to achieve accurate results, the GC-C-IRMS method requires, among other things, (1) proper identification of the target substances, (2) proper quality control measures, (3) good chromatography (specifically, purified material) and (4) adherence to good laboratory procedures.

4. I have reviewed the document package in this case and related documents, the transcript of the hearing of *United States Anti-Doping Agency v. Floyd Landis*, held on May 13 – 23, 2007 and the resulting Award of the Majority and the Dissent, the exhibits in that case and the pleadings and briefs in this appeal and the underlying case. These documents all reference the testing conducted at the Laboratorie National de Depistage et Dopage ("LNDD") in France.

5. I am being paid $2,000 plus travel expenses, which are nominal, for my participation in this case. This is far below what I normally would charge for this kind of case and the time I have spent reviewing these materials and testifying. I am participating in this

appeal proceeding at this drastically reduced rate because I believe that to uphold an anti-doping sanction on the evidence in this case is morally and ethically wrong.

6. After a review of the files and records and laboratory documents in this case, I have concluded that the GC-C-IRMS test results allegedly supporting an adverse analytic finding against Floyd Landis in the above-captioned case, including the GC-C-IRMS results for Stage 17 and other stages from the 2006 Tour de France, are inaccurate and unreliable and of no scientific worth.

THE CARBON ISOTOPE RATIO TEST

7. The purpose of the CIR test is to determine whether synthetic (exogeneous) testosterone is present in the urine sample. The test works by detecting the ratio of Carbon 13 to Carbon 12 present in testosterone. All testosterone (natural and synthetic) is composed of carbon. However, synthetic testosterone, made from soy plants, has far less Carbon-13 then the testosterone produced naturally in the human body. By comparing the ratios of Carbon-13 to Carbon-12 in the urine sample, scientists, theoretically, are able to determine whether synthetic (exogenuous) testosterone has been ingested.

8. The CIR test measures the isotopic ratios in four metabolites of testosterone. Metabolites are derived form testosterone once it is processed in the body. The CIR test detects the following metabolites: Androsterone ("Andro"), Etiocholanolone ("Etio"), 5a-Androstanediol ("5 Alpha") and 5B-Androstanediol ("5-Beta"). The Carbon-13 to Carbon-12 ratios in the metabolites will be the same as what was present in testosterone before the body broke it down.

9. Several factors, such as diet, can make the levels of Carbon-13 in the metabolites naturally low. To account for these variations, the CIR test compares the Carbon-13 to Carbon-

12 ratio of the metabolites to the same ratio of an endogenous reference compound ("ERC"). An ERC is a compound produced naturally by the body and is not affected by the introduction of synthetic (exogenuous) testosterone.

10. To accurately measure the ratio of Carbon-13 to Carbon-12 for each metabolite, the test must first be able to clearly identify each metabolite in the urine sample. The test does this by running the sample through a Gas Chromotgraph / Mass Spectrometer. The Gas Chromotograph passes the metabolites through columns coated with various hydrocarbon coatings. Each metabolite will pass through the column at a different rate, depending on how it interacts with the hydrocarbon stationary phase. These times are called retention times, or the time it takes for the compounds to exit the Gas Chromatograph column. Once they emerge through the tubes, the metabolites are ionized, and the mass spectrometer measures each metabolite's mass-to-charge ratio. The scientist can then assign each specific metabolite a retention time for passing through a Gas Chromotograph.

11. To measure the Carbon-13 to Carbon-12 ratio, the scientist will introduce the metabolite into a Gas Chromotograph followed by an Isotope Ratio Mass Spectrometer ("IRMS"). Instead of measuring the mass-to-charge ratio like the Mass Spectrometer, the IRMS measures the ratio of carbon isotopes in CO2 derived form the combusted sample. The IRMS is very simple. It essentially combusts (with heat and oxygen) the components of a sample after they pass through the Gas Chromotograph. The metabolites (more precisely the Carbon-13 and Carbon-12 in each metabolite) react with oxygen to form carbon dioxide (CO2). The insturment measures the ratio of Carbon-13 to Carbon-12 in the CO2 produced by each metabolite.

12. Theoretically, a laboratory can identify each metabolite that produced a certain Carbon-13 to Carbon-12 ratio in the IRMS by comparing it to the results of the Gas

Chromotograph and Mass Spectrometer (GC-MS) test. The GC-MS test used mass-to-charge to identify each metabolite with a known retention time. Since the GC-IRMS test also passes the metabolites through a Gas Chromtograph, each substance in the sample should have a retention time similar to the GC-MS test (although many variables may cause a change in a metabolite's retention time as discussed below). Therefore, by using retention time, the scientist can assign the Carbon-13 to Carbon-12 CIR ratio to a specific metabolite that was initially identified using GC/MS.

13. After the scientist assigns the Carbon-13 to Carbon-12 ratio to each metabolite, the scientist subtracts that value from the naturally occurring ratios of Carbon-13 to Carbon 12 measured in the ERC. That value (called the delta-delta value) is compared to the criteria (a delta-delta threshold) set out by WADA. If the delta-delta value for a certain metabolite is greater than the threshold set forth by WADA, the scientist can determine theoretically, for purposes of a doping violation, whether the sample contained synthetic testosterone.

LNDD'S ALLEGED QUALITY CONTROLS ARE OF NO VALUE

14. As the director of a laboratory, I am keenly aware of the importance of quality controls in connection with accurate CIR test results. If performed properly, quality control measures ensure precise, accurate and reliable testing and thereby provides the necessary assurances that the GC/C/IRMS instrument is functioning properly and accurately.

I have reviewed ISL 5.4.7.3 (Assuring the Quality of Test Results). ISL 5.4.7.3 states:

> Analytical performance should be monitored by operating quality control schemes appropriate to the type and frequency of testing performed by the Laboratory. The range of quality control activities includes:
>
> - Positive and negative controls analyzed in the same analytical run as the Presumptive Adverse Analytical Finding Sample.

As explained more fully below, I believe that LNDD violated ISL 5.4.7.3 because it had no meaningful positive and negative controls. Further, and independent of ISL 5.4.7.3, I conclude that the measures described by LNDD as "quality controls" provide no assurance of accuracy, do not function as true quality controls and provide no assurance that the GC-C-IRMS results are accurate and reliable, especially for the Stage 17 Sample. I believe that the quality control measures provide no benefit to USADA in its attempt to prove that it has presented evidence of a doping violation to the "comfortable satisfaction" of the hearing body.

15. In the Appellee Response Brief, USADA suggests that the quality controls of LNDD in this case provide the necessary assurances of accuracy, Appellee Response Brief, at 29-35. This is wrong. After reviewing the quality controls as described in the Appellee Response Brief, and the relevant documents, I conclude that the quality controls in this case provide no assurance that the GC-C-IRMS results are accurate and reliable, especially for the Stage 17 Sample. I believe that the quality control measures provide no benefit to USADA in its attempt to prove that it has presented evidence of a doping violation to the "comfortable satisfaction" of the hearing body. As I will describe further, the failure of the quality control measures in this case is particularly troubling in connection with the other laboratory failures in this case, including (1) failed identification, (2) poor chromatography, (3) manual processing errors, (4) deleted data and (5) other ISL rule violations.

16. USADA has consistently identified four quality control measures. These are (1) internal standard 5 alpha-androstanol acetate, (2) negative control "blank urine," (3) positive control "mix cal acetate" and (4) an instrument performance check. Appellee Response Brief, at *id.*, USADA's Pre-Hearing Brief ¶¶ 53-58, Ex. B to USADA's Response to Second Request for

Production of Documents ¶ 4 at 8. None of these measures provide any quality control assurance.

The Internal Standard: 5 Alpha-Androstanol AC

17. The use of the internal standard 5 alpha-androstanol acetate ("5 Alpha AC") provided no quality control assurance and it is a mistake to rely upon it for any purpose related to assuring the Panel that the results were accurate or reliable. Indeed, the contrary is true. 5 Alpha AC was added to the Mix Cal Acetate, as well as to every Sample Fraction ("F1, F2, F3") and Blank Urine Fraction (Blank Urine 1, Blank Urine 2, Blank Urine 3; hereinafter "BLU 1, BLU2, BLU3") with a known isotopic value.

18. The purpose of including 5 Alpha AC in the Mix Cal Acetate is to verify the accuracy of the GC-C-IRMS instrument.

19. If LNDD's testing process was accurate and reliable, LNDD should have identified 5 Alpha AC at a theoretic delta value of -30.46, within a measurement of error as stated by LNDD of ±0.5 delta units. *See* Ex. 24, USADA0175.

20. The Internal Standard 5 Alpha AC, a reference standard with a certified isotopic value, provided no quality assurance because LNDD could not determine its isotopic value within its declared acceptable range of error in four instances during the testing of Sample 995474. The exhibit prepared by Dr. Meier-Augenstein demonstrates that 5 Alpha AC was measured outside of its acceptable isotopic values. *See* Meier-Augenstein Presentation at Slides 52, 54; Closing Presentation at Slides 39, 40, 134, 136. The fact that LNDD failed to properly determine the isotopic values of 5 Alpha AC – the internal standard – within its measurement of uncertainty is strong evidence that LNDD's IRMS testing was variable and unreliable , because it can not even properly identify isotopic ratio in a pure solvent, which should be routine.

(Maurice, measurement variability is precision not accuracy. I tried to maintain proper scientific definitions while keeping your point largely in tact)

21. In the context of this case, it does not matter that there were some instances in which some of the Internal Standard 5 Alpha ACs were within the stated measurement of error of 0.5 delta units of the delta value of -30.46. In my opinion, it was out of this stated measure far too many times – four times out of 12 in the testing of Sample 995474 to give me any assurance that the instrument was operating properly.

22. I further comment that the statement by the AAA Panel in Paragraph 195 regarding the internal standard is nonsensical. In that paragraph, the AAA Panel stated that the internal standard's sole purpose was use as a chromatographic standard and therefore it was somehow unnecessary for LNDD to properly calculate the isotopic value of the internal standard. This makes no sense at all. If the internal standard is run, for whatever stated reason, LNDD should be able to properly calculate its isotopic value within the applicable measure of uncertainty. Inability to do so – especially as often as occurred here – indicates something was very wrong with the GC/C/IRMS instrument or the CIR test as performed by LNDD. In addition, the fact that LNDD has a specification for delta value precision suggests that it is certainly intended to be used as an isotopic standard.

23. Furthermore, and even contradicting the AAA Panel and its reasoning, on direct examination, USADA's own expert, Dr. Brenna, testified that: "It also has standards that have been – a standard that has been added to every sample that elutes early, and that standard is further checked to determine that the instrument is running properly during analysis of every particular sample." Tr. of Proceeding at 237.

Blank Urines Sample

24. Blank Urine Samples, or "negative controls," are designed to provide assurance that the CIR test is not determining a false positive. The Blank Urine Samples in this case as used by LNDD do not provide any such quality control assurance. As previously described, the internal standard 5 Alpha AC was determined to be outside of the measurement of uncertainty for the Sample B F3 fraction – the same fraction USADA relied upon to establish the AAF for Stage 17.

25. Furthermore, when the Blank Urine Samples were reprocessed on May 4 – 5, 2007 pursuant to this Panel's discovery order, the results provided no assurance that the GC/C/IRMS instrument was operating with sufficient accuracy and reliability such that the Blank Urine Samples were of any value. The reprocessing involved running the same data files for Sample 995474 pursuant to four different processing results: (1) the GC-C-IRMS' automatic feature, (2) reprocessing using the same "manual" technique, (3) reprocessing with zero background subtraction and (4) reprocessing according to Masslynx. The reprocessing yielded different results, and sometimes dramatically different results, for each of the target metabolites of testosterone in Sample 995474, for both Sample A and Sample B. *See* Exhibit GDC 01350, Closing Presentation Slide 113.

26. Upon reprocessing, the B Sample 5 alpha, when measured with automatic processing, went from -1.6 delta-delta to -3.45 delta-delta, and the A Sample 5 alpha went from -1.59 delta-delta to -3.65 delta-delta. The delta-delta variances between manual processing and automatic processing are too great (more than a 2 per mil difference) to provide any assurance that the blank urine provided effective quality control. The variation in analysis of biological samples in this case yields errors that are too extreme to be reliable for doping analysis. This is

especially important given that these blank urine fractions are the same fractions USADA relied upon to establish the AAF.

27. I have read the AAA Panel's opinion with respect to blank urine, in Paragraphs 202 to 205, and disagree with that analysis in its entirety. Whether or not the inconsistent figures are directly related to 5 alpha is not the point – the point is whether the blank urine variances are so great as to render it useless as a quality control. In my opinion, the failure of LNDD to be able to reproduce the results in the Blank Urine Samples using the same method in fact renders it a useless quality control.

28. Second, I note that Dr. Brenna in fact expressed concern over the reprocessing results. Dr. Brenna testified that he would have been concerned with the results of the manual reprocessing in the fractions themselves, at Tr. of Proceedings at 892-93.

Mix Cal Acetate Cannot Serve as a Positive Control

29. The purpose of a Positive Control is to ensure that the CIR test does not arrive at a false negative and does so, theoretically, by challenging the CIR test with a known positive. The Mix Cal Acetate mixture in this case as used by LNDD does not constitute effective positive control or quality control in this case. Mix Cal Acetate consists of four (4) steroid standards: (1) the internal standard 5 Alpha AC, (2) Etiocholanolone AC, (3) 5 Beta Androstandiol Di-AC and (4) 11 keto-etiocholanolone AC. Each of these acetate standards has an established isotopic value.

30. Mix Cal Acetate cannot serve as a positive control in this case because of several independent reasons. First, the Mix Cal Acetate solution is a non-complex matrix, unlike urine. Mix Cal Acetate preparation is a "clean matrix." As such, it contains only 5 Alpha AC, Etiocholanolone AC, 5 Beta Androstanediol diAC, 11-keto-etio AC in a solvent. A solvent is

chemically pure. In short, there are no other unidentified substances in the Mix Cal Acetate that could create the interference that is routinely seen in the actual sample chromatograms in this case. In contrast, urine is an exceptionally complex matrix that varies from person to person and under conditions of extreme exercise, which means that it contains a number of unidentified compounds that can create matrix interference. As a result, the chromatograms for the Mix Cal Acetate show no matrix interference, and the test results of the Mix Cal Acetate provide no assurance that LNDD can accurately identify or determine the isotopic values of the compounds in urine (a highly complex matrix). This is particularly true here, where the chromatography in the actual blanks and fractions is poor. *See* Ex. 24, USADA0173; Ex. 25, USADA0349. Indeed, USADA has argued that the addition of this matrix interference in the biological samples is why the internal standard cannot be quantified accurately in the blank and sample fractions. Appellee's Brief at 62. In making this conclusion, I agree with Dr. Meier-Augenstein's testimony that conducting a chromatographic analysis of the Mix Cal Acetate is like "shooting fish in a barrel," unlike the related analysis of human samples. Tr. of R. at 1452:8-13.

31. Second, the Mix Cal Acetate cannot serve as a positive control because it did not go through the LNDD sample preparation process. In order to be a true positive control, the Mix Cal Acetate must go through the sample preparation process in order to render accurate results of a known positive substance.

32. Third, Mix Cal Acetate does not contain three of the six target analytes necessary to quantify isotopic value in this case. In order to properly serve as a positive control, it would be necessary to have all six target analytes. These are: (1) 5 alpha androstandiol, (2) 5 beta androstandiol, (3) androsterone, (4) etiocholanalone, (5) pregnandiol and (6) 11 ketoetiocholanalone. Instead, the Mix Cal Acetate is missing 5 Alpha, Pdiol and Andro.

Without these, the isotopic value of the target analytes can not be determined, especially in the F3 fraction. Without these three key target analytes, only one of the three delta-delta values, Etio – 11-ketoetio, can be determined. Etio – 11-ketoetio, for both the A Sample and the B Sample, was never an issue in this case because the delta-delta values were -2.58 and -2.02, respectively.

33. Fourth, to be an effective positive control, the isotopic values of the target analytes must be what you would expect in a positive sample. More simply, the isotopic values of andro, etio, 5 alpha and 5 beta should be in the approximate range of negative 28 delta units and the isotopic values of pregnandiol and 11 keto-etio should be in the range of negative 23 delta units.

34. In making this conclusion, I disagree with the AAA Award at paragraphs 209 to 211, which suggests that "the situation of a 'dirty' matrix can only work effectively as a positive control when detecting an exogenous substance. Testosterone is not such a substance." AAA Award ¶ 209-11. This makes no sense. In the detection of testosterone in a doping case, testosterone is derivatized prior to analysis, thereby, making it an exogenous substance. Further, the contention that steroids from different origins would be mixed and therefore render a positive control unusable is nonsensical because that is what occurs, theoretically, if a person were to take testosterone – the endogenous testosterone in the body is mixed with the administered testosterone. In order to make a true positive control, the laboratory could spike urine with known amounts of synthetic metabolites to create a positive control. If for some reason, they find this method unsatisfactory, they could conduct an in vivo administration of testosterone in humans or animals and collect the urine. Another method would be to remove the testosterone from urine and then replace the components with a desired isotope ratio. Synthetic urine, or urine from individuals with lower levels of testosterone could also be used. Indeed, there is

absolutely no concern with mixing the endogenous testosterone metabolites with synthetic testosterone – because when creating a true positive control, the laboratory is capable of stripping urine of its endogenous steroids (ie., removing naturally occurring testosterone from the urine). Even after the urine is stripped, it is still a complex matrix, unlike the solvent mixture that is Cal Mix Acetate. In fact, LNDD knows how to do this. The positive controls in the T/E test show that LNDD is fully capable of creating positive controls in a urine matrix when testing for endogenous substances. This is true because LNDD's T/E positive controls were in fact stripped of endogenous testosterone metabolites.

LNDD's Instrument Checks Provided No Quality Control Assurance

35. As for quality control, I would also point out that LNDD has set for itself a very low acceptance standard for its quality control methods. In SOP ECC-10, LNDD sets forth its acceptance standard for Cal Mix IRMS. In ECC-10, LNDD sets a standard deviation of only 3 of 4 alkanes to be within LNDD's stated +/- 0.5 delta units. These four alkanes (decane, undecane, dodecane and methyldeconate) are in a pure matrix and thus extraordinarily easy to measure. This is inexplicable. If LNDD cannot measure all four of these alkanes within its own determined measurement of uncertainty, then its ability to properly measure the isotopic value of a substance in a dirty matrix with high background and interference from neighboring peaks is nil. In 1995, I measured a similar standard and made replicate injections of two different concentrations over a 4 day period achieving 1SD<0.2 per mil variation for 118 injections. Also, for the work I presented, isotope ratios were calculated using default parameters for vendor-supplied software, not manual integration. LNDD's acceptable error is more than twice what I was able to achieve for almost 40 times the number of injections over a significantly longer timeframe. *See* Goodman 1988: "Hardware Modifications to an Isotope Ratio Mass

Spectrometer Continuous-Flow Interface Yielding Improved Signal, Resolution, and Maintenance", K.J. Goodman, Analytical Chemistry, 70, 833-837, 1998.

36. The same is true for the Mix Cal Acetate. There, LNDD again states that only 3 of 4 of its steroid acetates must be within its stated error of +/- 0.5 delta units. Again, this is inexplicable. Inability to measure all four steroid acetates in a pure matrix within its stated measurement of uncertainty would lead me to believe that LNDD was incapable of properly measuring the isotopic value of a substance in a dirty matrix with high background and interference from neighboring peaks.

37. My opinion that the quality control measures in this case are meaningless is also supported by the way in which they were conducted. I note that USADA emphasizes that there is an IRMS injection sequence – involving the injection of three (3) stability runs, three (3) Mix Cal IRMS runs, Mix Cal Acetate, Blank Urine F3, F3, Blank Urine F1, F1, Blank urine F2, F2, and Mix Cal Acetate.

38. I have read that USADA, in both its AAA panel pre-hearing and reply briefs, emphasized that quality controls were run "immediately before and immediately after" or "minutes before and minutes after" Mr. Landis' A and B Samples. *See* USADA Pre-Hearing Brief ¶ 79 ("The Mix Cal Acetate results from the controls run immediately before and immediately after Respondent's A and B samples . . . ."); USADA Response Brief ¶ 27 ("In its Pre-Hearing Brief, USADA went into considerable detail to explain how the Mix Cal Acetate, Blank Urine and Mix Cal IRMS controls run in the same sequence **minutes before, during, and minutes after Respondent's sample**. . . .) (emphasis added). This is not true.

39. As Dr. Meier-Augenstein made clear in his testimony there was a five hour, fourteen minute gap between the running of the Sample A F2 fraction of Sample 995474, Ex. 24,

USADA0166, and the running of the Mix Cal Acetate. Ex. 24, USADA0183. The summary chart can be seen at Closing Presentation at Slide 42.

40. Dr. Meier-Augenstein also made clear that there was a four hour, forty minute gap between the running of the first Mix Cal Acetate, Ex. 25, USADA0362, and the running of the Sample B F3 Blank Urine of Sample 995474. Ex. 25, USADA0347. The summary chart can be seen at Closing Presentation at Slide 45.

41. I also have seen that in the transcript, LNDD lab personnel, Ms. Mongongu, when pressed to explain these gaps, testified that she forgot to add the Mix Cal Acetate to the A Sample. Tr. of R. at 600:20-601:3. Ms. Mongongu also testified that she could not remember what happened during the gap in the testing of the B Sample. Tr. of R. at 608:5-8. However, Ms. Frelat testified that the gap in the "B" sample occurred because she ran the initial quality controls, i.e., the stability, Mix Cal IRMS and Mix Cal Acetate, approximately four and one-half hours before Mr. Landis' "B" sample was prepared and ready for injection.

42. In totality, these extraordinary gaps and lax procedures give me no assurance in the accuracy or reliability of LNDD's quality control, and its test results in this case generally.

43. Lastly, LNDD's instrument checks provided no quality control assurance. In particular, USADA indicates that the stability runs do not provide any meaningful assurance that the GC-C-IRMS instrument can properly measure the isotopic value of any of the target analytes. The stability runs consist solely of three injections of CO2 gas. The CO2 gas is injected after the combustion phase – so it only tests the mass spectrometer. In effect, the injection of CO2 gas can only ensure that there are no leaks or other gross problems in the mass spectrometer or the general conditions of the system. It cannot ensure that the final isotopic values of GC combustion samples derived from a biological matrix are correct and proper.

IDENTIFICATION

44. One of the most critical components of GC-C-IRMS analysis is the proper identification of testosterone's metabolites. Without the proper identification of these metabolites, the GC-C-IRMS test results are utterly meaningless because there is no assurance that the isotopic values are even related to testosterone. In other words, without proper identification of testosterone's metabolites, the laboratory cannot provide this Panel with any assurance that what is being analyzed is in fact testosterone-derived metabolites. Indeed, ISO/IEC 17025 section 5.4.5.2 states: "The laboratory shall validate non-standard methods, laboratory-designed/developed methods, standard methods used outside their intended scope, and amplifications and modifications of standard methods to confirm that the methods are fit for the intended use. The validation shall be as extensive as is necessary to meet the needs of the given application or field of application. The laboratory shall record the results obtained, the procedure used for the validation, and a statement as to whether the method is fit for the intended use."

45. In my opinion, LNDD failed to properly identify testosterone's metabolites in Sample 995474 such that the test results in this case are unreliable, inaccurate and of no evidentiary value. I find that the procedures used by LNDD are in violation of WADA TD2003IDCR. Further, I find that, even aside from being in violation of WADA TD2003IDCR, the procedures used by LNDD are far outside good laboratory procedure and are utterly unreliable. Lastly, I conclude that LNDD's and USADA's statements about the identification of testosterone metabolites in this case are inexplicable and nonsensical. In order to fully explain this conclusion, I will begin with an explanation of IRMS testing.

46. I have read the statements by USADA from the AAA's Pre-Trial Hearing Brief and the statements in USADA's Appellee Response Brief regarding retention time and relative

retention time and I find USADA's statements logically inconsistent. Moreover, I find that the statements in USADA's Appellee Response Brief of the manner in which identification was conducted are scientifically invalid, inaccurate, unreliable and further, at odds with previous statements made by USADA and LNDD technicians about how identification of testosterone metabolites is conducted at LNDD. In addition, the methodology used is not in accordance with competent laboratory practice as described in ISO/IEC 17025 section 5.4.5.2 provided below. Non-standard methods need to be evaluated and verified in a systematic manner prior to employing them on real samples. It is not appropriate to invent and apply methodology on-the-fly.

47. The theory behind the IRMS test rests on the difference in the isotopic charateristics of carbon of naturally produced (endogenous) or synthetically produced (exogenous) testosterone. Testosterone is composed of Carbon, Oxygen and Hydrogen atoms. However, there are several isotopes of Carbon, including the stable isotopes ^{12}C and ^{13}C. Testosterone and its metabolites are composed of a mixture of ^{13}C and ^{12}C. The ratio of ^{13}C to ^{12}C in any individual will vary based on their source. For example, synthetically produced testosterone where is produced from soy plants, which are relatively low in ^{13}C, also known as ^{13}C depleted, compared to natural testosterone where ^{13}C enrichment is derived from, and varies according to, dietary sources. Thus, a person who uses synthetic testosterone or eats foodstuffs derived from a soy or wheat based diet will have testosterone with fewer ^{13}C atoms. In the context of anti-doping, the IRMS instrument measures the ratio of ^{13}C to ^{12}C, also known as the isotopic ratio or isotopic value, in specific metabolites of testosterone, as explained below.

48. The IRMS test does not measure the isotopic ratio of testosterone – it examines the metabolized products ("metabolites") of testosterone. The IRMS test measures the following

four metabolites of testosterone: Androsterone ("Andro"), Etiocholanolone ("Etio"), 5α-Androstanediol ("5 Alpha") and 5β-Androstanediol ("5 Beta"). The carbon framework of the testosterone metabolites will maintain essentially the same isotopic value as the testosterone from which they originated, according to the limited research conducted in this area mainly on non-atheletes. Therefore, the prevailing theory is that measuring the isotopic ratio of the metabolites is tantamount to measuring the isotopic ratio of testosterone.

49. There are several individual variables that can cause endogenous testosterone and its metabolites to become ^{13}C depleted that are unrelated to using exogenous testosterone, such as diet. To account for these individual variables, the IRMS test compares the $^{13}C/^{12}C$ ratio of a testosterone metabolite to the $^{13}C/^{12}C$ ratio of an endogenous reference compound ("ERC"). Comparing the difference in the $^{13}C/^{12}C$ ratio between a testosterone metabolite and an ERC, if performed properly, indicates the likelihood of testosterone being from an exogenous source.

50. In theory, for any individual at any one time the $^{13}C/^{12}C$ ratio of an ERC should be close to that of a testosterone metabolite. If a person is using exogenous testosterone, however, there will be a detectable and significant difference between the $^{13}C/^{12}C$ ratio in a testosterone metabolite and an ERC. In other words, if a person is taking exogenous testosterone, his or her $^{13}C/^{12}C$ ratio for a testosterone metabolite will be different than the ratio for an ERC.

51. That there is some detectable difference between the $^{13}C/^{12}C$ ratio between the metabolite and the ERC does not result in a positive test, however. Once the $^{13}C/^{12}C$ ratio for the ERC is subtracted from the testosterone metabolite, referred to as the $\delta^{13}C‰$ value or the delta-delta value, it must be compared to the positivity criteria mandated by WADA. The WADA positivity criteria for IRMS is as follows:

> The results will be reported as consistent with the administration of a steroid when the $^{13}C/^{12}C$ value measured for the **metabolite(s)** differs significantly i.e. by 3 delta units or more from that of the urinary reference steroid chosen. In some *Samples*, the measure of the $^{13}C/^{12}C$ value of the urinary reference steroid(s) may not be possible due to their low concentration. The results of such analysis will be reported as "inconclusive" unless the ratio measured for the metabolite(s) is below -28‰ based on non-derivatized steroid.

See Exhibit WADA0011-0021, at 3.

52. There are several metabolites whose isotopic values are measured by the IRMS instrument (Androsterone, Etiocholanolone, 5α-Androstanediol ("5α-Adiol") and 5β-Androstanediol ("5β-Adiol"), along with the isotopic value of two ERCs (11-Ketoetio and 5β-Pdiol). LNDD in theory identifies and measures all of these metabolites and ERCs. However, the relevant delta-delta numbers are calculated by subtracting the delta value of 11-Ketoetio (ERC) from the delta value of Etiocholanolone and Androsterone (metabolites) and from subtracting the delta value of 5β-Pdiol (ERC) from the delta value of 5β-Adiol and 5α-Adiol (metabolites).

How The Carbon Isotope Ratio ("CIR") Test Operates

53. The IRMS test consists of three main steps: (1) sample preparation, (2) pre-IRMS compound identification by GC/MS and (3) IRMS analysis. Each one of these steps must be performed properly in order to obtain accurate delta-delta values.

54. The IRMS test begins with sample preparation. First, an aliquot is made from the sample; additionally, an aliquot made from blank urine, which is taken from a pool of urine known not to contain synthetic testosterone (it is often the urine pooled from lab technicians). These aliquots are then cleaned through several physical, enzymatic and chemical treatments. The reason for this step is obvious – urine is a waste product, a "dirty" matrix, in which many other substances, in addition to testosterone and its metabolites, will be present. In order to

ensure the accuracy of the IRMS results, the sample must be stripped of those other substances so that it is clear that the laboratory is not measuring/analyzing the wrong substances.

55. The aliquots are then separated into three fractions using further physical treatments. The three fractions created are as follows: (1) the F1 fraction, containing 11-Ketoetiocholanolone (11-Keto), (2) the F2 fraction, containing Etiocholanolone (Etio) and Androsterone (Andro) and (3) the F3 fraction, containing 5α-Androstanediol (5α-Adiol), 5ß-Androstanediol (5ß Adiol) and 5ß Pregnanediol (5ß Pdiol). One of the last steps in sample preparation is the addition of an "internal standard." The internal standard, which in this case was 5 Alpha Androstanol Acetate, is a substance with a known isotopic value. Per LNDD, it allegedly serves as a quality control.

The IRMS Test

56. The IRMS test relies on two different instruments - the GC/MS instrument for accurate compound identification in the sample and the GC/C/IRMS instrument for determination of carbon isotope ratio in those compounds identified by GC/MS. Two instruments are needed because neither instrument can perform both the necessary functions to complete the test – identification and measurement. The GC/MS instrument cannot measure natural variation in isotopic values, it can only measure molecular mass; whereas, the GC/C/IRMS instrument can measure natural variation in isotopic values, but combusts all analytes to CO2 prior to detection so requires independent confirmation of the identity of the molecule. (Maurice, IRMS can measure molecular mass, it measures the mass of CO2). In some IRMS laboratories, the GC/MS instrument is attached to, and part of, the IRMS instrument. However, at LNDD, two different and non-attached instruments were used.

The GC/MS Analysis: Compound Identification

57. Once the fractions are prepared, the first phase of IRMS testing – compound identification with the GC/MS instrument – begins. The GC/MS instrument is composed of two major components: the gas chromatograph and the mass spectrometer. The gas chromatograph is used to separate molecules by sending these molecules through a column, which is essentially a tube coated with complex hydrocarbons. This coating is called the "stationary phase." Based on the interaction of each individual molecule with the stationary phase, each compound moves through the column at different rates. The amount of time each molecule takes to move through the column is that molecule's retention time. The fastest moving molecules reach the end of the column first, thus corresponding with the first peak in the chromatogram. The next fastest molecule follows and creates another peak in the chromatogram. This process continues until all of the remaining compounds have left the column.

58. Different molecules can have the same retention times, however. Therefore, after each molecule's retention time is measured, they are passed to the mass spectrometer. The molecules are passed through a stream of electrons. Electrons passing near to, or contacting, the analyte result in one or more electrons being dislodged from the molecule in question. This process, known as ionization, results in the molecule becoming "charged". A charged molecule is known as an ion. There are typically a number of different ions created in this process, the parent ion and fragment ions. Parent ions are intact molecules that have simply lost one or more electrons during ionization. Fragment ions are small pieces or "fragments" of the parent ion broken off during the process of ionization. Once ionized, the mass spectrometer measures the abundance of the different ions, also called a response, using each ionized mass-to-charge (m/z) ratio. This is akin to a molecular fingerprint, and is recorded by the mass spectrometer.

59. The GC/MS test produces a series of documents called chromatograms. The chromatogram shows all molecules within a designated m/z ratio. The chromatogram is simply a graph with time on the X-axis and response, or quantity, on the Y-axis. On the chromatogram, there are several peaks, each of which should correspond to a single compound in the sample. In sum, the GC/MS chromatogram identifies compounds by their retention times and m/z ratios.

Step 3: IRMS Analysis

60. After the identification of all of the target metabolites pursuant to the GC/MS analysis, the individual fractions are then injected into the GC/C/IRMS instrument. Once the fraction is injected into the GC/C/IRMS instrument, the compounds in the fraction are separated by gas chromatography. Similar to the GC/MS test, these molecules travel through a column and their retention times are recorded. However, unlike in the GC/MS instrument, after the molecules reach the end of the column, the molecules are combusted CO_2 in the combustion furnace. Only carbon dioxide remains after this step and there is no longer any means to measure the m/z ratio of the intact molecule. , The resulting carbon dioxide is then analyzed by the isotope ratio mass spectrometer, which determines with high precision the carbon isotope ratio of the combusted analyte. This analysis then determines the compound's isotopic value.

61. Although the only matrix containing samples that are injected into the GC/C/IRMS instrument described above is the fractions and blank urine, there are several other non-matrix samples introduced into the IRMS machine during the testing process. These include stability samples, Mix Cal IRMS samples, and Mix Cal Acetate samples and are analyzed as follows: (1) Stability run 1, (2) Stability run 2, (3) Stability run 3, (4) Mix Cal IRMS 003-1, (5) Mix Cal IRMS 003-2, (6) Mix Cal IRMS 003-3, (7) Mix Cal Acetate, (8) Blank Urine fraction

F3, (9) Sample F3 fraction, (10) Blank Urine F1 fraction, (11) Sample F1 fraction, (12) Blank Urine F2 fraction, (13) Sample F2 fraction and (14) Mix Cal Acetate.

62. The Mix Cal IRMS is a mixture of four reference standard alkanes: decane, undecane, dodecane and methyldeconate.

63. The Mix Cal Acetate contains four standard reference steroids with arbitrarily defined but different delta values. This sample also serves to test the ability of the IRMS instrument to measure delta values over a range comprised by the CIR test.

Retention Time and Relative Retention Time: WADA TD2003IDCR

64. Specifically, the GC/MS phase can only identify the testosterone metabolites. The GC/C/IRMS phase can only calculate isotopic ratios. Therefore, before a calculation of the isotopic ratios can be performed, the testosterone metabolites must be identified. This identification, of course, is critical.

65. WADA Technical Document TD2003IDCR, titled "Identification Criteria for Qualitative Assays Incorporating Chromatography and Mass Spectrometry," states that: "The Laboratory must establish criteria for identification of a compound."

66. In reviewing the testimony at the AAA proceeding, LNDD's discovery responses and USADA's briefs from the AAA proceeding, it is apparent to me that LNDD uses a relative retention time method for identification. I conclude this because of the following.

67. I have read the testimony of Appellee's witnesses, who have indicated that LNDD uses relative retention time to identify testosterone's metabolites. Those witnesses are as follows:

-- At the AAA hearing, Cynthia Mongongu, an LNDD lab technician, testified that LNDD added an internal standard to the blank urine and to the

athlete's sample "to calculate the relative retention time of the molecules analyzed." Tr. of R. at 653:8-10. Ms. Mongongu was asked whether the purpose of relative retention time was "to make sure that you're looking at the right peaks." *Id.* at 653:11-13. To which she replied, "Absolutely, Yes." *Id.*

-- Dr. J. Thomas Brenna's testimony at the AAA hearing also supports the importance of retention time and relative retention time. In describing the identification method for compounds in GC/C/IRMS, Brenna testified that LNDD's GC/C/IRMS chromatograms "have retention times that match . . . the previous GC/MS, and the GC/MS delivers structural information, like aliquots and so forth, that tell us which is which." *Id.* at 255:18-22. He further testified:

> . . . 171 is a GC/MS run which was shown 22 this morning, before lunch, and it is of Sample 995474, Fraction 3, so it's exactly the sample that is of interest here. And there are three peaks of particular interest. There is the 5-beta, the 5-alpha and the pdiol, which is the ERC --
>
> Q. Okay. And then, could you tell me what 173 is?
>
> A. -- 173, which I think is also here somewhere -- but in any case, 173 is the GC combustion version of that same chromatogram, that same sample. Sorry, the GC combustion -- IRMS. Sorry. We've been calling it the IRMS. I apologize. The IRMS version of that.
>
> Q. And what are the three peaks of interest there?
>
> A. Same three.
>
> Q. And how would I know --
>
> A. 5-alpha, 5-beta --
>
> Q. And how would I know which is which, because they just have numbers at the top.
>
> A. Well, they have retention times that match on the previous -- with the previous GC/MS, and the GC/MS delivers structural information, like aliquots and so forth, that tell us which is which.

-- Lastly, at the AAA hearing, Montreal WADA Lab expert witness, Dr. Christiane Ayotte testified:

Q. Did you hear Ms. Mongongu testify yesterday that the Paris lab runs an internal standard -- I think it's 5 alpha andro-stenediol --

A. Androstanol.

Q. Thank you -- to -- for the purpose of identifying retention times?

A. Yes, I heard her.

Q. Okay. And does the Montreal laboratory have an internal standard that you run for that same purpose?

A. It's good practice to add in each assay a standard to determine the relative retention time of your analytes, the substance that you will -- that you will wish to measure after. It's common and very good practice, so we have the same -- as a matter of fact, we have the same substance as a standard for that purpose.[1]

Dr. Ayotte continued:

A. But I'd say on the contrary, it's -- it's necessary to establish the relative retention time. It's a necessity; otherwise, you don't know what you are measuring, so . . . .[2]
(...)

Q. So just so I can be clear as to what your testimony is: **In this case, the IRMS analysis, what is the purpose of the internal standard, in your opinion?**

A. In that -- in their procedure, that standard, that, as a matter of fact, is added after several steps of the preparation, is used to establish the relative retention times.[3]

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1 Tr. of Proceeding at 811:23-812:18.

2 Tr. of Proceeding at 813:3-6.

3 Tr. of Proceeding at 849:20-850:2.

68. USADA's brief also specifically asserted that LNDD used retention time and relative retention time to properly identify the metabolites of testosterone in the IRMS test for Sample 995474. USADA's brief states, in relevant part:

> The second of the three steps in the LNDD test is pre-IRMS compound identification by GC/MS, the gold standard for compound identification in analytical chemistry applications. GC separates the compounds present in a mixture and MS identifies them. The first element of compound identification is the GC "retention time (RT)" and the second one is the molecular fingerprint recorded by the MS, which fragments the molecule into ions. Compound identification is achieved by matching GC retention times and MS ion patterns (Ion ratios) between the compound in the sample and a reference standard. . . .
>
> A parameter that is even better than the retention time is the relative retention time (RRT). It relies on the internal standard that was added to each tube during sample preparation. The internal standard has its own characteristic retention time. The relative retention time of any other compound is simply (RT of other compound)/(RT of internal standard). This makes comparisons of retention times easier because it normalizes them.

See USADA's Pre-Hearing Brief ¶¶ 41-42.

69. I would like to now explain the concepts of retention time and relative retention time. In order to ensure that isotopic ratios for the correct metabolites in question are being measured, a comparison must be made of the chromatograms that have resulted from the GC/MS phase and the GC/C/IRMS phase. This process must compare the peaks in the chromatograms resulting from the GC/MS phase (that identify the substances) to the peaks in the GC/C/IRMS phase (that provides the isotopic value). Retention time and relative retention time makes this comparison between the peaks by the amount of time that the molecules have taken to exit the GC column to the mass detector. Time is the only constant between the GC/MS phase and the GC/C/IRMS phase of the test.

70. Retention time is the amount of time it takes a molecule to travel through the GC column. The reason that retention time can be used to identify compounds in the two phases of

the IRMS test is that, because under constant chromatographic conditions, the retention time of a compound is reproducible. Thus, assuming that identical chromatographic conditions exist in both phases, the absolute retention times should be the same. *See International Union of Pure and Applied Chemistry* (IUPAC), chapter 9, section 9.2.3.7 "Retention Parameters in Column Chromatography, relative retention requires conditions to be the same and, specifically, the gradient." page 4, at http://www.iupac.org/publications/analytical_compendium/Cha09sec237.pdf.

71. The major problem of the use of retention time to identify compounds is the necessity of maintaining "exactly identical chromatographic conditions." A subtle temperature difference of 1 °C, a slightly increased carrier gas pressure, a larger column, or a few seconds of delay when starting the acquisition may cause retention time deviations.

72. Relative retention time is a way to improve the ability to choose target analytes in complex chromatograms when run under identical conditions. It is calculated by dividing the retention time of the target analytes (in this case, 5 alpha, 5 beta, Andro, Etio, 11-ketioetio and Pdiol) by the retention time of a known internal standard (in this case, 5αAndrostanol Acetate). In other words, the compound's retention time is anchored by the internal standard. Relative retention time thus helps normalize the variations between systems (because any change in the retention time will have an equal effect on both) and relative retention times can be used to compare between different systems.

73. Appellee's brief contends that relative retention time is not sufficient to identify the target analytes. This is correct. The only way to compare different systems is to run a linear hydrocarbon standard under linear gradient conditions as required by the Kovats formula. *See*

http://chromatographyonline.findpharma.com/lcgc/The-Challenges-of-Changing-Retention-Times-in-GCnd/ArticleStandard/Article/detail/445107?searchString=kovats.

74. In order to be certain that the laboratory staff are calculating the isotopic values of the correct peak, TD2003IDCR requires that the retention time of the peaks from the GC/MS process fall within specified time periods of each other: plus or minus 0.2 minutes or 1%, whichever is smaller. Without conforming to this requirement, there is no way to be certain that the peaks selected by the technician in the IRMS chromatographs are in fact the peaks that were previously identified as the target compounds (e.g., 5 Alpha, 5 Beta, Andro, Etio, 11-ketoetio and Pdiol). *See* Tr. of R. at 1400:1-1419:3. Specifically, WADA TD2003IDCR states that:

> For capillary gas chromatography, the retention time (RT) of the analyte shall not differ by more than one percent or ± 0.2 minutes (whichever is smaller) from that of the same substance in a spiked urine sample, Reference Collection sample, or Reference Material analyzed contemporaneously.

Exs. GDC00396-00400.

75. Although the AAA Award was flawed in almost every critical respect, even the AAA Award recognized the fundamental application of WADA TD2003IDCR. Paragraph 179 of the AAA Award states:

> What [WADA TD2003IDCR] does is to ensure that the technician is calculating the isotopic values of the correct peak. The Technical Document requires that the retention time of the peaks from the GC/MS part of the CIR test process falls within specified time periods of each other: plus or minus .2 minutes or 1%, whichever is smaller. Without this requirement, there is no way to be certain that the peaks selected by the technician in the IRMS chromatographs are in fact the peaks that were previously identified as the target compounds (e.g. 5 Alpha, 5 Beta, Andro, Etiocholanolone ("Etio"), 11-ketoetio and Pdiol).

76. The differences in the retention time and relative retention time of the target analytes in the GC/MS phase and the GC/C/IRMS phase of the IRMS test of Appellant's Sample A and Sample B from Sample 995474 were well in excess of the differences permitted by

WADA TD2003IDCR. In some cases, the difference in the relative retention time was nearly nine times the permitted difference. This is an enormous difference and well outside any properly laboratory procedures. I agree with the figures presented in the Presentation of Dr. Meier-Augenstein ("Meier-Augenstein Presentation") at Slide 24; Closing Presentation at Slide 26.

77. Further, and most importantly, even absent TD2003IDCR, these great variances in relative retention time (and retention time), and the corresponding violation of TD2003IDCR, are not a mere technicality, but rather directly affected whether LNDD properly identified the target metabolites of testosterone in this case. Simply put, LNDD cannot establish that the isotopic values used to support the AAF were indeed from a testosterone metabolite – the isotopic values could be from a substance that bears no relation to any of the target anayltes (and therefore no relation to testosterone). The failure to properly identify these target analytes renders LNDD's IRMS test results unreliable and inaccurate.

78. I have also reviewed Appellee's Brief, at pages 50 to 53, containing the description of how identification is conducted at LNDD. I believe that this description in Appellee's brief differs from the statements and testimony referenced above. I also note that this argument is an interpretation of Dr. Brenna's testimony, who is an outside expert and who has no additional information than that available to Appellant.

79. USADA's new argument is that LNDD uses the two injected substances from the Mix Cal Acetate, the 5 Alpha Androstanol AC and the 5 Beta Androstanol AC as a "retention time anchor" to identify the other peaks, and then uses "peak sequence and pattern to identify the additional peaks of interest." *See* Appellee's Brief at 51. USADA then goes on to say that this is a valid scientific method "the consistency of results in the subject samples." *Id.*

80. I disagree with this statement and method in its entirety.

81. First of all, claiming "consistency of results in the subject samples" somehow validates the method is unscientific and cannot be used to validate a scientific method. This action appears to be motivated by circular logic – that "we got what we expected so it must be right."

82. Secondly, this is not a procedure or parameter with scientific validity, such as retention time, that is set forth in WADA TD2003IDCR. Under TD2003IDCR, the laboratory must "establish criteria for identification of a compound." It then provides several acceptable examples, including the aforementioned retention time comparison. This newly invented and convoluted procedure was adopted by USADA after it was demonstrated that the method USADA claimed LNDD used (retention time and relative retention time analysis) – and which indeed LNDD itself claimed it used – failed, is not one of the enumerated examples. It is also not like anything found in the literature nor what any competent scientist would consider valid.

83. Lastly, and most importantly, it is utterly nonsensical when applied to this case. I have compared the "peak sequence and pattern" between the Mix Cal Acetate and the GC/C/IRMS chromatograms in this case, and there are no "peak sequence and patterns" that unambiguously match to help identify the substances in this case. Diagnostic tests should not rely on subjective analysis such as peak pattern matching, especially when other valid procedures exist. This was a failure of the laboratory to abide by its own operating procedures and it is trying to cover that mistake.

Visual Comparison of Peaks Between the GC/MS And IRMS Is Useless

84. It is also my opinion that there is no valid scientific basis for identification of substances by visually comparing peak heights between the GC/MS phase and the GC/IRMS

phase. I recognize that the AAA Panel has made reference to, that in this case, visual inspection of peak heights alone would allow a laboratory technician to make the necessary identification. Paragraph 186 of the Majority Award states:

> Instead, the lab compares the peaks and the sequence of the peaks from the GC/MS and GC/C/IRMS to identify the metabolites and the endogenous reference compounds. Specifically, to identify the substances in question, one would compare the pattern of peak heights and retention times in the GC/C/IRMS chromatograms, anchored by the internal standard with a known RT, with the pattern of peaks heights and RTs in the GC/MS chromatograms obtained from the same aliquot of the sample.

Majority Award, at Paragraph 186.

85. First, such an argument again ignores the fact that LNDD uses the GC/MS instrument as the means for identifying the target analytes. An "eyeballing" identification method is invalid. Comparison of peak heights from the GC/MS to GC/C/IRMS phases for purposes of identification is without any support in the science of IRMS or any other recognized standards. "Eyeballing" peak heights to try to identify the substances in the GC/MS phase with the substances in the GC/C/IRMS phase is illogical because the peak heights do not represent the same thing. In the GC/MS phase, peak heights are a function of ion current, whereas in the GC/C/IRMS phase, the peaks are proportional to the amount of carbon (in the form of CO_2) that has entered the ion source of the IRMS. These two measurements bear no relation to each other. Simply put, a technician cannot simply conclude that a "big" GC/MS peak is the same substance as a "big" GC/C/IRMS peak. Equally, a "little" GC/MS peak is not necessarily the same substance as a "little" GC/C/IRMS peak.

86. The AAA Panel's analysis, although not clear, appears to state that LNDD depends upon visual identification of the testosterone metabolites using a comparison of peak heights. I emphasize this method has no basis in good science, and therefore the conclusions

based on these flawed assumptions – that the differences in the RT and RRT were acceptable – must be rejected.

87. Furthermore, USADA's assertion in its brief that the similarity of the substances at issue means that the peak height comparison between GC/MS and GC/C/IRMS is available in this limited case is demonstrably wrong. As only one example, refer to the documentation package at USADA 0348 and USADA 0349 and in fact compare the peaks LNDD has designated as 5 Alpha AC, 5 beta diol, 5 alpha diol and Pdiol on the GC/MS and GC/C/IRMS. On the GC/MS, the internal standard peak is approximately one-half the height of the 5 beta diol and approximately the same height as the 5 alpha diol. The Pdiol peak is approximately two-thirds the height of the 5 beta diol peak. Compare that to the GC/C/IRMS. The peaks LNDD identifies as 5 alpha AC, 5 beta diol, 5 alpha diol and Pdiol do not, in fact, have the same relationship. In the IRMS chromatogram, the peak identified by LNDD as the internal standard 5 alpha AC is approximately the same as the peak it identifies as 5 beta diol. The peak identified as 5 alpha diol and the peak identified as Pdiol are now nearly the same height and both are approximately one-half the height of the peak identified as the 5 beta diol. Thus, when performing the peak height comparison suggested as possible by USADA, only the peaks identified by LNDD as 5 alpha diol and 5 beta diol on the IRMS bear a resemblance to the similarly identified peaks on the GC/MS.

The Importance of Method Files For GC/MS and IRMS Testing

88. I have reviewed the document package relating to Sample 995474. I conclude that if LNDD used a relative retention time analysis, the method files related to the IRMS instrument used to test Sample 995474 indicate that the conditions between the GC/MS and the GC/C/IRMS phases were such that the test results would be inaccurate, unreliable and of no

evidentiary value and would violate the generally accepted principles on the use of the IRMS test.

89. I will explain the importance of method files. To use retention time/relative retention time to identify compounds in a separate GC/MS instrument and IRMS instrument, it is critical that the conditions under which both GCs operate are the same. These conditions include a number of factors, but most importantly, temperature. Column length, column diameter, stationary phase, stationary phase thickness, and carrier gas flow also determine the time and in order which compounds will eluted, in other words, pass through the column, but temperature is the easiest parameter to change during analysis. Simply put, temperature is the primary variable that determines how long a given compound stays in the stationary phase. For any one compound, as a general rule, the higher the temperature, the less time a compound spends in the stationary phase.

90. Again, although relative retention time is a way to adjust for minor variations in instrument conditions, relative retention time analysis will not be able to overcome the huge differences in retention time that will be caused by having dramatically different method files and different columns.

91. The temperature and flow rate are conditions that are set in the GC method file. The method file is an electronic program that instructs the GC on all aspects of its operation. Therefore, in order to ensure proper identification in this case, the method files in the GC/MS and the GC/C/IRMS should have been identical, but they were not.

92. The method files for the GC/MS and the GC/C/IRMS runs that tested Sample 995474 show dramatically different conditions. For the GC/MS, the GC method files show the following:

- The column is held at 70 C for one minute;
- The temperature is then ramped up to 270 C, increasing 30 C every minute; and
- The temperature is then ramped up to 300 C, increasing 10 C every minute.

This dramatically differs from the method file for the GC/C/IRMS. For the GC/C/IRMS, the GC method file is as follows:

- The column is held at 70 C for one minute;
- The temperature is then ramped up to 270 C, increasing 30 C every minute;
- The temperature is then ramped up to 280 C, increasing 0.6 C every minute;
- The temperature is then held at 280 C for three minutes;
- The temperature is then ramped up to 300 C, increasing 5 C every minute; and
- The temperature is then held at 300 C for 5 minutes.

Notably, these programs are the same up until the temperature of each system reaches 270 C. After that, they differ dramatically. The result of this difference is that the RT and RRT (but not the order) of each eluant, or target analyte, are not comparable between the two systems. Again, the failure of LNDD to properly use its instruments has resulted in inaccurate and unreliable test results. Accuracy and reliability of a diagnostic test fails when it is left to the operator to make a subjective judgment.

LNDD's Document Package Indicates LNDD Used Different Columns In Its GC/MS And GC/C/IRMS Phases

93. I have reviewed the document package relating to Sample 995474, especially that part of it relating to the use of the columns in the GC/MS and GC/C/IRMS phases. The document package indicates that different columns were used in both phases.

94. I am aware that LNDD has suggested that the columns were the same, notwithstanding the information indicating to the contrary in the document package. I understand that LNDD only made this assertion (1) after Appellant submitted his brief indicating that the columns were different and (2) after the AAA Panel below found that using different columns would establish an ISL violation. At the outset, I find this "new discovery" deeply troubling, and extraordinarily convenient.

95. I would like to explain the significance of the use of two different columns in these two phases. First, the use of two different columns makes calculation of accurate relative retention times impossible. Second, the use of different columns may possibly cause the substances to elute at different times and in a different order. As a result, the different substances are going to appear in the GC/MS chromatogram and the GC/C/IRMS chromatogram at different times, thereby defeating the new (but scientifically invalid and unacceptable) "peak matching" technique now described by USADA in its Appellee's Brief.

96. The column is the piece of equipment in the gas chromatograph that performs the critical function of separating the compounds. Columns are manufactured by various makers, and are replaceable. When using separate GC/MS and GC/C/IRMS instruments, as was the case here, the columns must be identical if the chromatograms between the two phases are to be of any use in relation to each other.

97. The reason is simple – unless the columns are the same, the amount of time it takes for a compound to elute between the GC/MS and GC/C/IRMS will be so different that the retention times and relative retention times will not be comparable. Peer-reviewed papers have concluded that different columns can even change the order in which compounds leave the column. Identification of peaks in a complex matrix would further complicate this problem. *See*

Skogsberg, U. et al., Investigation of the Retention Behavior of Steroids with Calixarene-based Stationary Phases by Modern NMR Spectroscopy, *Journal of Separation of Science,* vol. 26, pl 1119-24 (2003).

98. Indeed, the Majority Panel apparently recognized the importance of using the same column in the GC/MS and GC/C/IRMS phases, because in attempting to support its conclusions, the Majority Panel explicitly stated, "The GC Column is, of course, the same in both instruments." Majority Award, at para. 186.

99. The document package related to Sample 995474 shows that this is untrue. In this case, LNDD used two different columns, with different characteristics. The column used in the GC/MS phase was Agilent 19091s-433. *See* USADA 0124, 0303.

Part Number	Description
19091S-433	HP-5MS, 0.25mm * 30m * 0.25um

Part number 19091s-433, as documented on USADA0124 and USADA0303, is the HP-5ms column, as documented at the Agilent website.[4]

100. Agilent describes its 19091s-433 column as a **non-polar** column with stationary phases comprised of 5% phenyl, 95% methyl-polysiloxane. However, the column used in the GC/C/IRMS phase was an Agilent DB-17ms column. *See* USADA 0153. The manufacturer classifies this column as a **midpolarity** column with stationary phases comprised of (50% phenyl)-methyl-polysiloxane.

101. Changes in polarity in the stationary phase of the column can affect changes in (1) compound retention time and (2) the order in which compounds elute from the column itself. *See* Skogsberg, U. et al., Investigation of the Retention Behavior of Steroids with Calixarene-

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[4] http://www.chem.agilent.com/ecommerce/product/Product_Catalog_3.aspx?prod_search=19091S-433&Pid=32486. Accessed Oct. 14, 2007.

based Stationary Phases by Modern NMR Spectroscopy, *Journal of Separation of Science,* vol. 26, p. 1119-24 (2003). Therefore, the use of the different columns rendered the IRMS test results inaccurate and unreliable and contributed to the impermissible differences in RT and RRT in this case.

102. Lastly, the use of two different columns is a separate and additional violation of LNDD's own SOP. The use of two different columns violates the LNDD's own Standard Operating Procedure ("SOP") governing T/E testing. LNDD's SOP governing GC/MS testing is LNDD SOP M-AN-52, Analyse GC/MS—Confirmation Qualitative des Metabolites de Testosterone et de les Precurseurs—LNDD 00664. It clearly indicates that the DB-17ms column be used. Indeed, this makes perfect sense because LNDD's accreditation documents require that for GC/C/IRMS analysis, the DB-17ms column be used. *See* LNDD0086 and LNDD 0098. These accreditation documents are from the months before and after the testing of Sample 995474. As made clear from LNDD's SOP and accreditation documents, LNDD itself recognizes that the same columns must be used in both the GC/MS and IRMS tests.

Mix Cal Acetate Is of No Help With Retention Time or Relative Retention Time

103. Further, USADA's attempt to overcome the retention time and relative retention time deficiencies in this case by asserting that Mix Cal Acetate can be used to calculate retention time or relative retention time is of no merit. USADA attempted to make this argument during the AAA case by calling Dr. Brenna on rebuttal on May 23, 2007. At that time, Dr. Brenna suggested that retention times could be calculated from the Mix Cal Acetate. Specifically, he stated:

> Q: I'm asking whether or not you can calculate the relative retention time off the mix cal acetate in this case. The mix cal acetate formulation used in this case. Yes or No?
>
> A. Yes.

Tr. of R. 1957:13-19.

104. However, Dr. Brenna was later forced to admit on cross-examination that his previous testimony was incorrect because it is not possible to calculate the relative retention time in this case from the Mix Cal Acetate. The reason is simple – the following metabolites – 5 Alpha, Pdiol, and Andro (which are the key metabolites) – are not in the Mix Cal Acetate. *Id.* at 1958:1-3. When this was pointed out to him, he admitted "you cannot calculate a relative retention time from the mix cal acetate . . . I'm sorry." Therefore, it is undisputed that the Mix Cal Acetate cannot be used to identify 5 Alpha, Andro and 5 Beta by relative retention time.

The AAA Panel Erred In Its Analysis of WADA TD2003IDCR

105. I have reviewed the AAA Award regarding the analysis of WADA TD2003IDCR and conclude that it erred. The Majority Panel, in finding that no ISL violation occurred with respect to retention time and relative retention time, found that the WADA TD2003IDCR does not apply to retention times from two instruments:

> However, it must be noted, **that TD2003IDCR does not apply to RRTs between two different and separate instruments that are not of the same type.** Therefore, Dr. Meier-Augenstein misdirected himself in his testimony before the Panel by comparing RRTs not between two GC/MS or two GC/C/IRMS instruments, but instead between one GC/MS and one GC/C/IRMS.

Majority Award, para. 182. Again, this is incorrect and without any support in the evidence produced at the arbitration, even by Appellee's own witnesses. First and foremost, the Panel's position that Dr. Meier-Augenstein's analysis was incorrect is contradicted by (1) the Panel's own statement at paragraph 179, (2) Appellee's witnesses, (3) Appellant's witnesses, and (4) USADA's briefs. Most importantly, from a scientific standpoint, the fundamental reasoning of the Majority Panel is incorrect.

106. In finding that TD2003IDCR does not apply, the Majority Panel stated that "two different instruments" could not have comparable retention times/relative retention times due to the length of "plumbing" in the GC/C/IRMS instrument. Indeed the Majority Panel stated that:

> After the sample passes through the GC portion of the GC/C/IRMS system there is an additional length of plumbing in the GC/C/IRMS machine adding a significant amount of time to the total RT of the substance.

Majority Award, at para. 184. Indeed, the Majority Panel provides the following hypothetical to illustrate its point:

> The additional time added to the RT of the analyte or standard in the IRMS will always be a constant time, regardless of the individual substances or compounds being measured. Consequently, the retention times of the compounds emerging from the GC/MS system cannot be the same as those coming from the GC/C/IRMS. Likewise, the RRTs will also be different. Taking the example used above, **if the RT from the GC/MS is 10 min for the target analyte and 5 min for the internal standard, in the case of IRMS, we may be adding an additional 1 minute for the combustion of those compounds to take place**. The reason that the additional time is the same for each substance/compound is that the substance or compound is no longer in its original form; they have been combusted completely to form CO2. As such, the RT for the target analyte at the end of the IRMS would be 11 min and the RT for the internal standard is 6 min. This results in a RRT of 11/6. Arithmetically speaking it is not possible for the RTs and the RRTs to be identical in the GC/MS and GC/IRMS systems nor can it be ensured that it will be within TD2003IDCR.

Majority Award, at para. 185.

107. The "plumbing" referred to by the Majority Panel is the tubing that connects the GC to the combustion chamber to the IRMS; it does not contain any stationary phase. Because there is no stationary phase, all substances pass through this "plumbing" at the same rate.

108. The AAA Panel is incorrect that different "plumbing" will cause the differing amount of retention times seen in this case. Moreover, the current assertion by USADA that relative retention time – and the GC/MS phase – is not used for identification does not make any sense. First, as noted above, the technicians have said that LNDD uses relative retention time

analysis. But moreover, if LNDD is not using GC/MS for this purpose (to identify the testosterone metabolites), it is entirely unclear why it would run the GC/MS test.

109. Further, there is a well-established scientific practice to account for the plumbing in the GC/C/IRMS instrument which, because the additional time is a constant, is to simply subtract the period of time that the compounds travel through the additional length of plumbing from the retention times of the compounds. Simply put, the retention time of the GC/C/IRMS phase is determined by subtracting the time the compounds spend in the additional length of plumbing. This function is performed automatically by the OS2 software. By default the software is set to subtract 30 seconds, but this can be changed by the operator to reflect the actual amount of time that is added. Dr. Davis indicated that he checked this figure and that it was set to the proper amount. This procedure, known as "building the adjusted retention time," resolves entirely the phantom issue raised by the Majority Panel.

110. Moreover, the Majority Panel's hypothetical does not support the conclusion that TD2003IDCR does not apply to two different instruments. It simply means that proper procedure must be followed with respect to the calculation of relative retention time. It is well-accepted that the "hold-up time" (called "delay time" in the OS2 software) – the time that is used by the compound traveling through the "plumbing" – is a constant time that is subtracted from the retention time when calculating relative retention time. Thus, in the hypothetical above, the 1 minute would have been subtracted, thereby allowing a comparison of 10 minutes to 10 minutes for the target analyte and 5 minutes to 5 minutes for the internal standard. The Majority Panel's Award reflects a fundamental misunderstanding of proper procedure as it relates to relative retention time.

111. In summary, LNDD failed to identify: (1) 5αAndrostanediol ("5 Alpha"), (2) Androsterone ("Andro") and (3) Pregnandiol ("Pdiol") in any test associated with Sample 995474 using either retention time or relative retention time. For Sample 995474, without proper identification of (1) 5 Alpha, (2) Andro and (3) Pdiol, the following delta-delta values for Sample 995474 cannot be determined: (1) 5 Alpha – Pdiol, (2) 5ßAndrostanediol ("5 Beta") – Pdiol and (3) Andro – 11-ketoetiocholanolone ("11 ketoetio"). These, of course, are the delta/delta values that LNDD now alleges support an adverse analytic finding against Mr. Landis.

112. Without this, or any other appropriate method of identification, the isotopic values found by LNDD for Sample 995474 are inaccurate, unreliable and have no evidentiary value. I similarly conclude that the isotopic values found by LNDD for all the other allegedly positive GC-C-IRMS tests in this case are inaccurate, unreliable and have no evidentiary value.

CHROMATOGRAPHY

113. To begin with, I would like to explain what chromatograms are. A chromatogram (for both the GC/MS test and the GC/C/IRMS test – both parts of the IRMS test) is a graphic representation of the signal intensity data obtained from the sample. In these tests, the chromatograms have retention time on the x-axis, and signal intensity on the y-axis. The chromatograms are the foundation for the analysis and calculations that occur during the test. Accordingly, the quality of the chromatogram affects the reliability and accuracy of the later calculations, and ultimately, the test results. Put differently, if the quality of the chromatogram is poor, even if the later calculations are performed properly, the test result will be inaccurate and unreliable.

114. I have reviewed all of the relevant chromatograms in this case supporting the adverse analytic finding from Sample 995474 and the other alleged positives attributed to

Appellant from the other stages of the Tour de France tested by LNDD. I conclude that the quality of those chromatograms is poor, and that they display matrix interference, coelution (the overlapping of peaks such that accurate determination of isotopic value is made impossible), high sloping baselines and other artifacts that make the determination of accurate isotope ratio calculations impossible.

115. I have also reviewed ISL 5.4.4.2.1 and conclude that LNDD violated ISL 5.4.4.2.1 by failing to properly generate chromatograms that avoided interference in the detection of the prohibited substance or its metabolites and markers by components of the sample matrix. The many violations of ISL 5.4.4.2.1, as seen in LNDD's poor chromatography in this case, require me to conclude that the test results are inaccurate, unreliable and utterly lacking any scientific or evidentiary value.

116. Moreover, and most importantly, regardless of the existence of ISL 5.4.4.2.1, the poor chromatography in this case is a violation of basic scientific principles governing the use of the GC/C/IRMS instrument, which renders the test results in this case inaccurate, unreliable and utterly unworthy of any scientific or evidentiary value.

117. There is overwhelming scientific support for the principle that good chromatography is critical to accurate IRMS results. Such support can be seen in the peer-reviewed literature referenced during Dr. Meier-Augenstein's testimony. *See* Meier-Augenstein Presentation at Slide 5; Ex. GDC01297.

118. An example of the dramatic effect that matrix interference and poor chromatography can have in the isotopic values is shown by the study of marine organisms described in Dr. Meier-Augenstein's presentation. *See* Meier-Augenstein Presentation at Slides 28-30.

119. I also agree with the testimony of Dr. Meier-Augenstein, who explained that even small coeluting peaks can have a substantial isotopic effect on larger peaks. An example of this occurred during the AAA proceeding, when, on cross-examination, Dr. Meier-Augenstein was asked to prepare a demonstrative exhibit. This demonstrative, Exhibit 120, proved that even a small coeluting peak could have more than a -2 per mil effect on the target peak, where the isotopic value of the smaller peak was a hypothetical -70 per mil.

120. Further, I find this compelling because, as Dr. Meier-Augenstein explained, the IRMS peaks in this case could have been incompletely combusted and the isotopic values of those peaks could be as low as -700 per mil. Tr. of Proceeding at 1488:14-1489:23. Indeed, as Dr. Meier-Augenstein pointed out, the isotopic values for the background were more negative than -120 per mil in several of Appellant's samples. Tr. of Proceeding at 1489:19-23.

IRMS TEST RESULTS: POOR CHROMATOGRAPHY

121. I have reviewed the following chromatograms and conclude that they are so poor that they are of no evidentiary value when attempting to analyze the testosterone metabolites in this case, and further they are unreliable and of no evidentiary value and violate generally accepted principles (including the ISL) relating to the GC/C/IRMS instrument testing:

a. The chromatogram at Exhibit 24, USADA0173 (Sample 995474, Sample A, Fraction 3). *See* Tr. of R. at 1433:18-1434:9.

b. The chromatogram at Exhibit 25, USADA0349 (Sample 995474, Sample B, Fraction 3). *See* Tr. of R. at 1416:9-1417:10.

c. Stage 11: The chromatogram at Exhibit 88, LNDD1110 (Sample B, Fraction 3). *See* Tr. of R. at 1848:7-1849:9.

d. Stage 15: The chromatogram at Exhibit 86, LNDD0894 (Sample B, Fraction 3). *See* Tr. of R. at 1850:23-1851:10.

e. Stage 19: The chromatogram at Exhibit 87, LNDD0991 (Sample B, Fraction 3). *See* Tr. of R. at 1851:11-1852:10.

f. Stage 20: The chromatogram at Exhibit 84, LNDD0704 (Sample B, Fraction 3). *See* Tr. of R. at 1852:11-1853:8.

g. I have focused my review on the foregoing chromatograms, which are all Fraction 3 chromatograms, because they contain the 5 Alpha, 5 Beta and Pregnandiol (including the internal standard). These are the target **metabolites** that USADA has focused on. However, I have also reviewed the Sample 995474 A and Sample 995474 B F1 and F2 fractions, which show similar chromatographic problems, as well as the F1 and F2 fractions for all the other stages cited by USADA as "corroborative evidence." These chromatograms are equally poor.

LNDD'S MANUAL PROCESSING OF TEST RESULTS

122. I have carefully reviewed the briefs and transcript from the AAA hearing regarding the "manual processing" or "manual integration process" (which terms are interchangeably used) and am able to conclude that the manual processing process performed by LNDD has no basis in good laboratory procedure or science and is a violation of the ISL. Further, I conclude that the manual processing performed by LNDD with respect to the samples in this case renders the results inaccurate, unreliable and of no evidentiary value.

123. I would like to begin by explaining manual processing. Manual processing, as described by LNDD and USADA, is the process by which the LNDD technician manipulates the peak start and end points that were defined by the complex algorithm in the GC/C/IRMS instrument. It also refers, in this case, to the process by which the laboratory technician, after the GC/C/IRMS instrument has subtracted the background, either adds or deletes points in the background. This manual processing can have a tremendous effect on the isotopic value, such

that it can cause the final delta-delta value to go from a negative to a positive. Manual processing, in other words, replaces the peak start and end points and the background points determined by the complex algorithms embedded in the GC/C/IRMS instrument.

124. This process is utterly objectionable because it replaces the determinations made by the complex algorithms embedded in the GC/C/IRMS instrument with the subjective judgments of individual laboratory technicians. As a principle, this kind of manual processing is not scientifically valid and any Carbon Isotope Ratio test results that were manually processed should be disregarded as unreliable and inaccurate.

125. Furthermore, as I have seen in this case, the expertise and judgment of the laboratory technicians in this case are extremely poor. They have demonstrated numerous instances of incompetence or lack of knowledge of the IRMS instrument, and even if manual processing were an acceptable technique, these technicians are clearly incompetent to do so. Examples of this incompetence are described in further detail below.

126. Before I can explain why manual processing, and in particular, the manual processing performed by LNDD, is inappropriate, some background is required. A chromatogram is a graphic representation of raw data, in other words, a series of numbers, obtained by the GC/C/IRMS instrument. However, the chromatogram does not graphically represent every data point that was obtained by the instrument. Instead, the chromatogram uses only some of the data points to create the graphic that is printed. For instance, even when the technician is reviewing the chromatogram zooming in on one of the target peaks, the chromatogram is only depicting about 10% of the data points associated with the particular peak. When the software embedded in the GC/C/IRMS instrument determines the peak integration and

the background subtraction, the complex algorithm is based on the entire data set, not just the data points contained in the chromatograms.

127. The isotopic ratio for a compound is calculated based on the representative peak in the chromatogram taking into account the background, which includes signal noise and impurities in the matrix. In calculating the isotopic ratio of a particular compound, defining the peak start and end points, peak integration, and subtracting the background is critical. Therefore, all GC/C/IRMS instruments are embedded with complex algorithms to determine where to define the peak start and end points and how to subtract the background.

128. Indeed, USADA in its discovery responses stated that the "Background Subtraction is embedded in the instrument software, which is proprietary to the instrument manufacturer. LNDD has no separate documentation." Ex. B to USADA's Response to Respondent's Second Request for Production of Documents ¶ 10 at 10; Ex. C to USADA's Response to Respondent's Second Request for Production of Documents ¶ 8 at 2. This is not true.

129. Based on the testimony I have reviewed during the AAA proceeding, LNDD technicians manually integrated the peaks and added and deleted background points in the chromatograms associated with Sample 995474. Not only did the LNDD technicians manually process the results, but they failed to record in any manner how they manipulated the data. By manually processing and not recording how the technicians manipulated the data, LNDD violated the ISL and generally accepted scientific principles and methodology. Accordingly, the Carbon Isotope Ratio test results are unreliable and inaccurate.

130. LNDD did not record, in any manner, how it altered the peak start and end points and which background points were added or deleted, and is impossible to review. The failure to

record this information is in violation of the ISL at §§ 5.4.4.1.4 and 5.2.6.1, ISO 17025, and generally accepted scientific practice, which all generally require that aspects of the analytical process be documented such that an independent analyst could reproduce the results. Because the technicians did not record how they manually processed the data, a competent analyst cannot reproduce the result. Indeed, as noted above, the same analyst could not reproduce previously submitted results. Further, without recording the changes to the peak integration and the background points, neither I, nor any other expert, can review the manual processing by the LNDD technicians. In light of the inexperience of the LNDD technicians, the evidence of other errors committed by LNDD technicians, the great variation in the results, and the lack of any ability to review the results, I conclude that the results are inaccurate and unreliable.

131. Further, despite it being contrary to generally accepted scientific principles and methodology, LNDD has an SOP describing the process by which its technicians should manually manipulate the results. LNDD 0605. The SOP states that the laboratory technician should review the 2/1 trace to determine where the peak start and end points should be. The 2/1 trace, however, has no demonstrated significance or correlation with the underlying peaks contained in the data set that is graphically represented by chromatograms. The 2/1 trace is an arbitrary graphical representation of the ratio between two of three signals measured by the IRMS, the 44 ion, which is ^{12}C plus two oxygen atoms, and the 45 ion, which is ^{13}C plus two oxygen(^{16}O). Unlike the chromatogram, which is a quantitative representation of signal produced by analyte combustion, which look like a series of humps, the graphic representation of the 2/1 ratio sometimes looks like a sideways "S," with the center line of the trace representing the ratio between the amplified signals (and detector offsets) for the 44 ion and the 45 ion beams. In essence, the SOP states that the peak start should be defined when the 2/1 trace begins to

move upward on the sideways "S" and it ends when the 2/1 trace completes the sideways "S" to return to the starting ratio. Simply put, the manual peak integration described by LNDD's SOP is not based on observing the raw data or the chromatogram generated by the GC/C/IRMS instrument, but rather is based on the 2/1 trace, which has no valid connection to the raw data from the sample or demonstrated improvement in identifying peak starts and stops for the purpose of integration.

132. That LNDD has an SOP permitting its technicians to manually alter the data does not make this manual processing scientifically appropriate. Indeed, the manual processing described in the SOP is not scientifically valid for numerous reasons. First, the 2/1 trace is a relic of the older dual inlet IRMS instruments before the GC/C/IRMS instrument was developed. The GC/C/IRMS instrument, unlike that of the dual inlet IRMS instrument, produces chromatograms similar to single channel HPLC or GC instruments. The 2/1 trace is of little to no value in the GC/C/IRMS instrument. What I mean by this is that the algorithms used by all GC/C/IRMS instruments to determine peak integration and the background points are based on the raw data from the detector, similar to HPLC and GC instruments. The 2/1 trace does not match or correlate with the peaks shown in the chromatogram in such a way that the 2/1 trace is used as a guide to determine the peak start and end points. By using the 2/1 trace to determine the peak integration, LNDD is using an orange to define a point on a pear. This simply cannot be done and should not be done.

133. Critically, by engaging in manually processing, LNDD is essentially introducing human subjectivity in place of a complex computer algorithm that is capable of reproducibility determining peak integration parameters based on well-established and scientifically sound criteria. This is nonsensical. Further, that LNDD operators were following a scientifically

invalid SOP does not change my conclusion or alter the fact that LNDD introduced human subjectivity into its analysis. A majority of the funding in the isotope ratio mass spectrometer field is being spent on developing better algorithms to identify the peaks. Indeed, Dr. Brenna has spent a great deal of his research time in the past years evaluating and creating algorithms that can better integrate the peaks and subtract the background, including a paper I co-authored with him. That LNDD disregards the algorithm in the GC/C/IRMS instrument to use what at best can be described as a "trivially simple" and scientifically invalid method of manual peak integration and background subtraction is remarkable. Moreover, the chromatogram displayed on the screen does not necessarily represent all of the data points associated with a particular chromatographic peak. Therefore, when the peak is manually integrated, a slight movement of the peak start or end point may disregard a significant amount of the relevant data. If it was generally accepted scientific practice to engage in this manual processing, the research in the area of developing better algorithms, in which both Dr. Brenna and I were involved, would be superfluous.

134. Also, the interjection of subjectivity into this analysis is questionable, because as we have seen in this case, this manual processing does not lead to reproducible results. Reproducibility is of paramount importance in science. If test results cannot be reproduced, the results are not reliable and have little evidentiary value. Indeed, in this case, we see that by using the manual processing, the Carbon Isotope Ratio test results cannot be reproduced. It is my understanding that the raw data from the Carbon Isotope Ratio test of Sample 995474 was reprocessed at the LNDD laboratory in May 2007. The difference between the delta-delta values for some of the target analytes from the original test and the reprocessed tests stand in start contrast with each other. The difference between the the 5-alpha minus P-Diol on Mr. Landis' "A" from the original test run and the reprocessed run is .81‰. The difference in the delta-delta

values in the "B" sample are even worse. The delta-delta value for the Etio minus 11-keto is 1.67‰, the Andro minus 11-keto is 1.90‰, and the 5-alpha minus P-Diol is .80‰. GDC 1350. Indeed, Dr. Brenna testified in the Appealed Case that the difference in the results would cause him concern. Tr. of R. 359:17-24. These results support the fact that when manual processing is used, the results are not reproducible. Without any reproducibility, the results are not reliable and clearly establish the scientific fallibility of the method.

135. Moreover, during the AAA proceeding, USADA's witnesses repeatedly asserted that manual processing was a quality control. This is not true. The manual processing performed by LNDD should not and cannot be considered a mechanism of quality control or be considered some form of peak integration optimization. As discussed above, a quality control sample or action is used to verify that the instrument is working properly and within specified limits. If the quality control does not pass its standard, the problem that led to the failed quality control should be corrected, and the assay should be repeated, if possible. If the technician believes that the software did not properly integrate the peak, the error that led to this improper peak identification should have been corrected. For instance, as I have noted above, it is likely that the poor peak separation in the chromatograms led to the improper peak integration by the software. When the technician reviewed the peak integration and believed that it was in error, he or she should have corrected the error that led to the poor peak separation and re-run the sample or deem the sample invalid or out of specification. There is absolutely no scientific support for laboratory technician Claire Frelat (who had limited experience performing the CIR test), to make undocumented and arbitrary changes to the peak integration. Manually processing is not a method to correct poor chromatography. There is no reason to believe that human subjectivity can correct for poorly resolved peaks in the sample.

LNDD'S MANUAL PROCESSING OF THE QUALITY CONTROLS ESTABLISHES THAT ITS QUALITY CONTROLS ARE TRULY MEANINGLESS

136. A very telling indicator that LNDD's quality control process is a failure is that the batch summary sheets from the IRMS (found at USADA0155 for Sample A and USADA0331 for Sample B) report different values than the individual reports for each Mix Cal IRMS run. The batch summary sheet is the sheet that summarizes the individual reports sheets (found at USADA0178-0180 for the "A" and USADA0357-0359 for the "B"). There is no legitimate reason for different values to appear on the summary sheet than on the individual reports sheets. The reason for this occurrence is that LNDD ran, and then manually reprocessed, its "quality control runs." The fact that this is bad laboratory procedure cannot be overstated.

137. For both the A and B Samples, there was a summary page entitled "Batch Data Processing Results." This summary page contained values reflecting the individual test results from each of the tests conducted in the Sample A and Sample B sequences. For Sample A, the summary page is Exhibit 24, USADA0155. For Sample B, the summary page is Exhibit 25, USADA0359. In both the Sample A and the Sample B sequences, it is clear that LNDD cherry-picked the results that appear on the "Batch Data Processing Results" page. LNDD's manipulation is clear because the individual test results on the "Batch Data Processing Results" page do not match the results on the individual test pages that were included in the document package.

138. For Sample A, the results of the Mix Cal IRMS 003-2, Exhibit 24, USADA0179, do not match the results shown on the "Batch Data Processing Results" page. Ex. 24, USADA0155. The original isotopic value of methyldeconate in this sample was -32.22. The value after LNDD manually reprocessed this data was -31.76. The original values of the other alkanes (decane, undecane and dodecane) are forever lost, as LNDD destroyed those records.

Whatever they were, however, they were different from the values LNDD ultimately used for its Mix Cal IRMS "quality control."

139. Likewise, the results of the Mix Cal IRMS 003-2, Exhibit 25, USADA0358, do not match the results shown on the "Batch Data Processing Results" page. Ex. 25, USADA0331. The original isotopic value of methyldeconate in this sample was -31.68. The value after LNDD manually reprocessed this data was -31.44. The original values of the other alkanes (decane, undecane and dodecane) are forever lost, as LNDD destroyed those records. Whatever they were, however, they were different from the values LNDD ultimately used for its Mix Cal IRMS "quality control."

140. For Sample B, the results of the Mix Cal IRMS 003-3, Exhibit 25, USADA0359, do not match the results shown on the "Batch Data Processing Results" page. Ex. 25, USADA0331. The original isotopic value of methyldeconate in this sample was -32.42. The value after LNDD manually reprocessed this data was -31.22. The original values of the other alkanes (decane, undecane and dodecane) are forever lost, as LNDD destroyed those records. Whatever they were, however, they were different from the values LNDD ultimately used for its Mix Cal IRMS "quality control."

141. USADA misunderstands the significance of this when it writes in its Appellee's Response Brief that "the reason for this difference is that the delta value shown in the injection sequence page (USADA0331) is recorded automatically by the instrument *before manual integration*." Appelle's Brief page 61 (emphasis added). USADA thus appears to excuse these differences because the laboratory technicians used manual reprocessing to change the values of the Mix Cal IRMS prior to the values appearing on the summary sheet. This is inexcusable.

142. USADA also is attempting to misdirect the Panel about the significance of the batch sheets with respect to the quality controls when it argues that "[t]he acquisition time for control samples and Appellant's samples are clearly reflected in the document packages. As such, there are no concerns that the instrument was not performing properly." Appellee's Brief at 58. The print time for the data sheets, not the acquisition time, is what establishes that LNDD manually processed the results.

143. The Mix Cal IRMS is a pure solution of four alkanes, and only four alkanes. Apart from the CO_2 pulses in the stability runs, nothing LNDD measures on the IRMS is easier to do correctly than the Mix Cal IRMS. Mix Cal IRMS is a pure solution that should produce four perfect and narrow peaks and only those four perfect peaks. In my opinion, LNDD's need to manually reprocess the Mix Cal IRMS – a pure mixture that is easy to properly determine isotopic values than anything else in the run except for stability runs – shows that LNDD is incapable of properly determining isotopic values of the testosterone metabolites in the urine matrix that follows it.

144. To be very clear on this point, in order to generate data that would satisfy LNDD's very loose quality control parameters, LNDD was, in this case, required to manually reprocess three of the six Mix Cal IRMS runs. This is in spite of the fact that the Mix Cal IRMS has no possibility of matrix interference and contains four, and only four, sharp, well defined peaks. That LNDD could not produce acceptable isotopic values without manipulating them manually provides clear evidence that LNDD's quality controls are providing no value and that it does not understand how to obtain accurate and reliable results using the vendor-supplied software.

DR. SIMON DAVIS' DECLARATION

145. I have reviewed the declaration of Dr. Simon Davis in its entirety and agree with all of the statements contained within the substantive portions of his declaration. Indeed, I would be perfectly comfortable in adopting those paragraphs as part of my declaration, but in order to prevent this declaration from being unnecessarily lengthy, I felt it was better to simply adopt the relevant paragraphs contained above.

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I declare under penalty of perjury under the laws of the United States of America that the foregoing is true and correct. This declaration was executed on March 7, 2008, in Boston, MA.

KEITH GOODMAN

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EXPERIENCE

2002–present **Xanthus Pharmaceuticals, Inc.** **Cambridge, MA**
Senior Director, Analytical Chemistry

- Assembled and managed a state-of-the-art R+D laboratory with MS and PhD level scientists.
- Designed and executed *in vitro* and *in vivo* experiments to evaluate drug metabolism and pharmacokinetics. Discovered novel metabolites derived from animal PK experiments.
- Developed analytical methods based on HPLC and LC MS/MS for internal use and to support GLP contractors.
- Co-authored an SBIR fast–track grant that received a 150 priority score and 2.1M budget.
- Researched and pursued new collaborative relationships to improve product portfolio.

2000–2002 **Boyce Thompson Institute** **Ithaca, NY**
Manager, Technical Services

- Managed a laboratory dedicated to stable isotope analysis funded to profitability through user fees and grant support.
- Served as a consultant to students and faculty on how to design, implement, and interpret studies involving stable isotopes.
- Researched and developed new applications for isotope ratio analysis.

1996–2000 **Metabolic Solutions, Inc.** **Nashua, NH**
Senior Staff Scientist

- Developed an FDA approved assay for the detection of Helicobacter pylori from 13CO2 derived from orally ingested 13C-urea.
- Prepared documentation for an NDA for Helicosol and 510K for the accompanying urea (breath or blood) test.
- Researched and authored three NIH SBIR grants with awards totaling 1.25 million dollars.
- Managed research and collaborative relationships in support of SBIR grants.
- Developed US patent 6,548,043: "Measurement of gastric emptying"

EXPERIENCE (Cont.)

1999 **United States Track and Field** **Indianapolis, IN**

Consultant

- Audited preparation and analysis methods for the analysis of testosterone from urine.
- Testified as an expert witness in a doping case involving the use of isotope ratio mass spectrometry for the detection of synthetic testosterone in urine.

1995– 1996 **Premier American Technologies Co.** **Bellefonte, PA**

Senior Scientist

- Developed sample analysis interfaces for a commercial isotope ratio mass spectrometer.

Jan. 1995– Oct. 1995 **Iowa State University** **Ames, IA**

Research Associate, Department of Food Science and Nutrition

- Introduced new technologies and pursued research opportunities with collaborating laboratories.
- Designed and implemented an improved GC combustion interface for a commercial isotope ratio mass spectrometer.

EDUCATION

1989–1994 **Cornell University** **Ithaca, NY**

Major: Ph.D. Nutritional Biochemistry

Minors: Analytical Chemistry, Biophysical Chemistry.

- Thesis "Gas chromatography-combustion isotope ratio mass spectrometry for metabolic investigations using highly enriched [$U^{13}C$]-labeled precursors"
- Awarded National Institutes of Health Training Grant Jan. 92 –Dec. 95.
- Developed US Patent 5,661,038: "Interface System for Isotopic Analysis of Hydrogen"

1985–1989 **Binghamton University** **Binghamton, NY**

Harpur College, B.S. Chemistry

- Awarded "Distinguished Independent Study in Chemistry".
- Participated in the National Science Foundation Summer Research Program at UNC Chapel Hill, June-August 1988.

PROFESSIONAL AFFILIATIONS

Scientific Reviewer: Small Business Review Panel (SSS-6) at the NIH, February 26-27 2004.
Journal Reviewer: Current Organic Chemistry, Bentham Science Publishers.
Member: American Society of Mass Spectrometry (ASMS), American Chemical Society ACS), and The American Society for Pharmacology and Experimental Therapeutics (ASPET).

PUBLICATIONS

"Symadex, a FLT3 Kinase Inhibitor, is Metabolized by Aldehyde Oxidase" Goodman, KJ, Duncan, K, Locniskar, A., Ajami, A., *Drug Metabolism and Disposition,* in preparation 2008.

"Combination of phenotype assessments and CYP2C9-VKORC1 polymorphisms in the determination of Warfarin dose requirements in heavily medicated patients" V. Michaud, M-C. Vanier, D. Brouillette, D. Roy, L. Verret, N. Noel, I. Taillon, G. O'Hara, D. Gossard. M. Champagne, K. Goodman, Y. Renaud, A. Brown, M. Phillips, A.M. Ajami, J. Turgeon, *Clin. Pharmacol Ther.* Accepted September, 2007.

"Impaired Hepatic Mitochondrial Oxidation Using the 13C-methionine Breath Test in Patients With Macrovesicular Steatosis and Patients with Cirrhosis." Spahr L, Negro F, Leandro G, Marinescu O, Goodman KJ, Rubbia-Brandt L, Jordan M, Hadengue A., *Medical Science Monitor*, 2003 Jan;9(1):CR6-11.

"Acute Valproate-Associated Microvesicular Steatosis: Could the [13C]methionine Breath Test be Useful to Assess Liver Mitochondrial Function?" Spahr L, Negro F, Rubbia-Brandt L, Marinescu O, Goodman K, Jordan M, Frossard JL, Hadengue A., *Digestive Diseases & Sciences.* 2001 Dec;46(12):2758-61.

"Effect of Meal Size and Test Duration on Gastric Emptying and Gastric Myoelectrical Activity as Determined with Simultaneous [13C]octanoate Breath Test and Electrogastrography in Normal Subjects Using a Muffin Meal." Gonlachanvit S, Chey WD, Goodman KJ, Parkman HP. *Digestive Diseases & Sciences.* 2001 Dec;46(12):2643-50.

"Gastric Emptying Characteristics of a Novel ^{13}C-Octanoate Labelled Muffin Meal", W.D. Chey, B. Shapiro, A. Zawadski, K. Goodman, *Journal of Clinical Gastroenterology*, 32(5):394-399, 2001.

"Hardware Modifications to an Isotope Ratio Mass Spectrometer Continuous-Flow Interface Yielding Improved Signal, Resolution, and Maintenance", K.J. Goodman, *Analytical Chemistry*, 70, 833-837, 1998.

"Recycling of Carbon into Lipids Synthesized *De Novo* is a Quantitatively Important Pathway of [U-^{13}C]-α-Linolenate Utilization in the Developing Rat Brain" C.R. Menard, K.J. Goodman, T.N. Corso, J.T. Brenna, and S.C. Cunnane, *Journal of Neurochemistry*, , 71(5) 2151-2158, 1998.

"Assessing Metabolism of [^{13}C]β-carotene Using High Precision Isotope Ratio Mass Spectrometry", R.S. Parker, J.T. Brenna, J.E. Swanson, K.J. Goodman, B. Marmor, *Methods in Enzymology*, 282, 130-140, 1997.

"Interconversion of α-Linolenate to Long Chain and Non-essential Fatty Acids in the Perinatal Period of the Rhesus Monkey Studied Using [U-^{13}C]-Tracers and High Precision Gas Chromatography-Combustion Isotope Ratio Mass Spectrometry", R. Sheaff-Greiner, Q. Zhang, K.J. Goodman, D.A. Giussani, P.W. Nathanielsz, J.T. Brenna, *Journal of Lipid Research*, 37, 243-254, 1996.

"Evidence of *cis-trans* Isomerization of 9-*cis*-β-Carotene During Absorption in Humans" You, C-S., Parker, R.S., Goodman, K.J., Swanson, J.E., and Corso, T.N., *American Journal of Clinical Nutrition*, 64(2) 177-183, 1996.

"Experimental approaches to the study of beta-carotene metabolism: potential of a ^{13}C tracer approach to modeling beta-carotene kinetics in humans" Swanson, J.E., Wang, Y.Y., Goodman, K.J., and Parker, R.S., *Advances in Food and Nutrition Research* 40, 55-79, 1996.

"High precision D/H Measurement From Hydrogen Gas and Water by Continuous Flow Isotope Ratio Mass Spectrometry", H.J. Tobias, K.J. Goodman, C.E. Blacken, and J.T. Brenna, *Analytical Chemistry*, 67(14), 2486-2492, 1995.

PUBLICATIONS (Cont.)

"High Precision Gas Chromatography-Combustion Isotope Ratio Mass Spectrometry at Low Signal Levels", K.J. Goodman, J.T. Brenna, *Journal of Chromatography* A, 689, 63-68, 1995.

"Curve Fitting for Restoration of Accuracy for Overlapping peaks in Gas Chromatography Combustion Isotope Ratio Mass Spectrometry", K.J. Goodman, J.T. Brenna, *Analytical Chemistry*, 66(8), 1294-1301, 1994.

"Study of β-Carotene Metabolism in Humans Using ^{13}C-β-Carotene and High Precision Isotope Ratio Mass Spectrometry", R.S. Parker, J.E. Swanson, B. Marmor, K.J. Goodman, A.B. Spielman, J. T. Brenna, S. M. Viereck, and W. K. Canfield, *Annals of the New York Academy of Sciences*, 691, 86-95, 1993.

"High Sensitivity Tracer Detection Using High Precision Gas Chromatography-Combustion Isotope Ratio Mass Spectrometry and Highly Enriched [U-^{13}C]-Labeled Precursors", K.J. Goodman and J. T. Brenna, *Analytical Chemistry*, 64(10), 1088-1095, 1992.

CONFERENCE ABSTRACTS

"Symadex, a FLT3 Kinase Inhibitor, is Metabolized by Aldehyde Oxidase" Goodman, KJ, Duncan, K, Locniskar, A., Ajami, A., Experimental Biology, April 5-April 9, 2008. Abstract accepted.

"Pharmacokinetics and Antitumor Activity of Demethylpenclomedine in Rodents"
J. Buluran, J.S. Paterson, K. Goodman, J. Christensen, M.Chau, Y. Maxuitenko, M.H. Falahatpisheh, R. Switzer III, A.M. Ajami and C.Grieshaber. Proceedings of the American Association for Cancer Research (AACR) 97th Annual Meeting, April 1-5, 2006, Abstract 3817.

"A Rapid and Sensitive LC-MS/MS Method for the Determination of C-1311 (Symadex™) and its Glucuronide Metabolite in Rat Plasma" K.J. Goodman, M. Chau, C.K. Grieshaber, and A. Ajami. 53rd Annual ASMS Meeting on Mass Spectrometry and Allied Topics, San Antonio, TX, 2005.

"A Rapid and Sensitive LC-MS/MS Method for the Determination of Amonafide and N-Acetyl Amonafide in Human Plasma", G. McRae, J. Bouchard, K. Goodman, M. Harvey, 52nd Annual ASMS Meeting on Mass Spectrometry and Allied Topics, Nashville, TN, 2004.

"Development and Validation of an LC-MS/MS Method for Quantification of Caffeine and Selected Metabolites for NAT2 Phenotype Determination", G. McRae, M.G. Boudakian, J. Bouchard, K. Goodman, M.D. Harvey. 51st Annual ASMS Meeting on Mass Spectrometry and Allied Topics, Montreal, QC, 2003.

"Effect of Meal Size and Test Duration on Myoelectrical Activity and Gastric Emptying as Determined by Electrogastrography (EGG) and ^{13}C-Octanoate Breath Test (OBT) ", S. Gonlachanvit, W. D. Chey, K. J. Goodman, and H. P. Parkman, Eighth International Workshop on Electrogastrography, San Diego, May 2000, Dig. Dis. Sci., 45:1246, 2000.

"Gastric Emptying Characteristics of a Novel ^{13}C-Octanoate Labelled Muffin Meal", W.D. Chey, B. Shapiro, A. Zawadski, K.J. Goodman, Digestive Diseases Week, Orlando, FL May 1999.

"An Evaluation of Peak Detect Algorithms for Samples at High ^{13}C Enrichment in Gas Chromatography-Combustion Isotope Ratio Mass Spectrometry." Goodman, K.J. and Brenna, J.T. 42nd Annual ASMS Meeting on Mass Spectrometry and Allied Topics, Chicago, IL 1994.

"Plasma Kinetics of a Small Oral Dose of ^{13}C-β-Carotene in Humans." J.E. Swanson, Y. Wang, R.S. Parker, W.K. Canfield, K.J. Goodman, and, J.T. Brenna. Mathematical Modeling in Exp. Nutrition V, Fort Wane, IN, May 1994.

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"Metabolism of 13C-β-Carotene in a Human Subject as a Function of Carrier Lipid." B. Marmor, R.S. Parker, J.E. Swanson, C.S. You, Y. Wang, K. Goodman, J.T. Brenna and W. Canfield. FASEB 94, Anaheim, CA, The FASEB Journal 8(4), A192 (1994).

"Metabolism of ^{13}C 9-cis β-Carotene in humans." C.S. You, R.S. Parker, K.J. Goodman, J.T. Brenna, and W. Canfield. FASEB 94, Anaheim, CA, The FASEB Journal 8(4), A422 (1994).

"Interconversion of α-Linolenic in Lactating rhesus monkey plasma and milk studied using perlabeled precursors and high precision gas chromatography-combustion isotope ratio mass spectrometry (GCC-IRMS)", Q. Zhang, K. J. Goodman, J. T. Brenna, P. W. Nathanielsz, Presented at Fatty Acids and Lipids from Cell Biology to Human Disease:1st International Congress of the International Society for the Study of Fatty Acids and Lipids, Lugano, July 1993.

"Metabolism of α-Linolenic Acid in Lactating Rhesus Monkeys Studied Using High Precision Gas Chromatography-Combustion Isotope Ratio Mass Spectrometry", Q. Zhang, K. J. Goodman, and J. T. Brenna, 41st Annual ASMS Meeting on Mass Spectrometry and Allied Topics, San Francisco, CA, 1993.

"Curve Fitting for Resolution of Overlapping Chromatographic Peaks in High Precision Gas Chromatography-Combustion Isotope Ratio Mass Spectrometry (GCC-IRMS)", K. J. Goodman and J.T. Brenna, 41st Annual ASMS Meeting on Mass Spectrometry and Allied Topics, San Francisco, CA, 1993.

"High Precision Gas Chromatography-Combustion Isotope Ratio Mass Spectrometry (GCC-IRMS) at Femtomole Carbon Levels and High Enrichments (δPDB>50 permil)", K. J. Goodman and J.T. Brenna, 41st Annual ASMS Meeting on Mass Spectrometry and Allied Topics, San Francisco, CA, 1993.

"High Precision Gas Chromatography-Combustion Isotope Ratio Mass Spectrometry and Highly Enriched ^{13}C-Labeled Tracers", J. T. Brenna and K. J. Goodman, Science Innovation 92, San Francisco, CA, 21-27 July 1992.

"Metabolism and Biokinetics of ^{13}C-β-Carotene in Humans Following a Small Oral Dose", R. S. Parker, S. M. Viereck, A. B. Spielman, J. T. Brenna, and K. J. Goodman, FASEB 92, Anaheim, CA, The FASEB Journal 6(5), A1645 (1992).

"Transport and Interconversion of γ-Linolenic and Docosahexaenoic Acids from Mother to Fetus in the Baboon Studied with Stable Isotopes and High Precision Isotope Ratio Monitoring Gas Chromatography", J. T. Brenna, K. J. Goodman, L. Houghton, P. W. Nathanielsz, FASEB 92, Anaheim, CA, The FASEB Journal 6(5), A1384 (1992).

"Fatty Acid Interconversion in Humans Studied Using ^{13}C-Perlabeled Precursors and High Precision Isotope Ratio Monitoring Gas Chromatography", J. T. Brenna, K. Goodman, 12th Int. Mass Spectrom. Conf., Amsterdam, Aug., 1991.

"High Precision Isotope Ratio Monitoring Gas Chromatography and Highly Enriched ^{13}C-Labeled Precursors for Investigations of Lipid Metabolism", J. T. Brenna, K. J. Goodman, 33rd International Union of Pure and Applied Chemistry Congress, Budapest, Hungary, August, 1991.

"Perlabeled Tracers and Gas Chromatography/Combustion/Gas Isotope Ratio Mass Spectrometry for High Sensitivity Metabolite Detection in Mammals", J. T. Brenna, K. Goodman, 39th Annual Conf. Mass Spectrom. Allied Topics, Nashville, TN, June, 1991.